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FORCED DRAINAGE OF THE CENTRAL NERVOUS SYSTEM

ITS EFFECT ON THE BLOOD AND ON THE CEREBROSPINAL FLUID *

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In 1926, Kubie [1] described a method for drainage of the central nervous system, which he believed might be effective in certain infections of the nervous system. In subsequent papers [2] the method was further elaborated, controlled by experiments on animals and applied to human beings.

The theory of the method is as follows: The cerebrospinal fluid is a dialysate derived from the blood plasma and is in hydrostatic and osmotic equilibrium with it. The cerebrospinal fluid is formed by a process of filtration through the capillaries of the choroid plexus and also through the capillaries throughout the central nervous system, the latter portion of the fluid draining into the subarachnoid space by way of the perivascular spaces. Drainage of the cerebrospinal fluid by lumbar puncture, therefore, should drain the perivascular spaces as well as the subarachnoid space and ventricles. The fluid formed from the choroid plexuses and the perivascular fluid may be increased either

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* Read at the Fifty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, May, 1929.

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1. Kubie, L. S.: Intracranial Pressure Changes During Forced Drainage of Central Nervous System, Arch. Neurol. & Psychiat. **16**:319 (Sept.) 1926.

2. Kubie, L. S., and Shults, G. M.: Bull. Johns Hopkins Hosp. **27**:91, 1925. Kubie, L. S.: Forced Drainage of the Cerebrospinal Fluid in Relation to the Treatment of Infections of the Central Nervous System, Arch. Neurol. & Psychiat. **19**:997 (June) 1928; The Intracranial Pressure in Health and Disease, New York, Paul B. Hoeber, 1929.

by raising the hydrostatic pressure in the capillaries or by rendering the blood hypotonic. From a theoretical consideration of these two methods, the latter should be by far the most effective.

By making the blood hypotonic either by intravenous injections of hypotonic salt solution or by the administration of water by mouth, during continuous drainage of the spinal fluid, Kubie believed that toxins and exudate may be washed from the perivascular spaces in the depths of the central nervous system, into the subarachnoid space, and thence discharged through the lumbar puncture needle.

The soundness of this treatment depends primarily on the correctness of the views in regard to the cerebrospinal fluid already expressed. These matters have been discussed extensively in three recent papers by one of us [3] and cannot be reviewed in detail here. The idea that the cerebrospinal fluid is a dialysate in equilibrium with the blood was first brought forward by Mestrezat [4] in 1912, based on the consideration of the physical and chemical properties of the cerebrospinal fluid. His strongest argument, that the blood plasma and cerebrospinal fluid have the same osmotic pressure as measured by depression of the freezing points, has been confirmed recently in our laboratory by Thomas [5] and also by Teschler.[6] Mestrezat and Ledebt [7] showed that if blood plasma and cerebrospinal fluid were separated by a dialysing membrane impermeable to protein, but freely permeable to the other constituents of plasma and cerebrospinal fluid, no change in the composition of the cerebrospinal fluid took place. Furthermore, in animal experiments they showed that a protein-free dialysate from the blood had essentially the same freezing point and composition as the cerebrospinal fluid of the animal. In 1923, Weed [8] showed that the formation and absorbtion of cerebrospinal fluid may be varied at will by changing the osmotic pressure of the blood, and his work demonstrated, furthermore, a communication between perivascular spaces of the brain and cord and the subarachnoid space. These facts are basic in consideration of Kubie's method.

There remains further to be shown that an increased flow of perivascular fluid may be promoted by rendering the blood hypotonic. In Weed's experiment, after the intravenous injection of distilled water, a marked increase in the cerebrospinal pressure took place, and

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3. Fremont-Smith, F.: Nature of Cerebrospinal Fluid, Arch. Neurol. & Psychiat. **17**:317 (March) 1927. Fremont-Smith, F., and Forbes, H. S.: Intra-Ocular and Intracranial Pressure, Arch. Neurol. & Psychiat. **18**:550 (Oct.) 1927.

4. Mestrezat, W.: Le liquide cephalorachidien, Paris, A. Maloin et fils, 1912.

5. Thomas, G. W.: Unpublished data, 1928.

6. Teschler, L.: Deutsche Ztschr. f. Nervenh. **103**:87, 1928.

7. Mestrezat, W., and Ledebt, S.: Compt. rend. Soc. de biol. **85**:55 and 81, 1921.

8. Weed, L. H.: Am. J. Anat. **32**:253, 1923.

histologic examination showed distention of the perivascular and perineuronal spaces. In 1929, Kubie[9] confirmed these observations and demonstrated further that when the spinal fluid is continuously drained throughout such an experiment, this distention of perivascular and perineuronal spaces does not occur. In other experiments[10] in which perivascular infiltration had been produced experimentally, extrusion of this exudate into the subarachnoid space was indicated when the blood was rendered hypotonic, during drainage of the cerebrospinal fluid.

From the foregoing considerations, it is evident that the theory of Kubie's treatment is sound. Kubie has already applied this method in the treatment for septic meningitis and anterior poliomyelitis. It was his suggestion[11] that it should be tried in multiple sclerosis.

In the treatment for multiple sclerosis, we have used the following slight modification of Kubie's method.

A lumbar puncture is performed on the patient after he has fasted over night, and the cerebrospinal fluid is drained at a zero or slightly negative pressure for approximately three hours. During this period, water is forced by mouth in amounts ranging from 500 to 1,000 cc. per hour. When water is given in such quantities a prompt diuresis ordinarily occurs, and little dilution of the blood takes place.[12] In order to accentuate the dilution of the blood, i. e., to render it more hypotonic, a subcutaneous injection of posterior lobe pituitary extract is given at the beginning of the treatment (0.5 cc. of vasopressin or 1.0 cc. of solution of pituitary). This delays the diuresis for a period of from four to six hours or longer, as first shown by Motzfeld,[13] and is given with the idea that a marked dilution of the blood following water drinking should take place under such circumstances.

It is our purpose to report the changes that occur in the blood and cerebrospinal fluid during such a procedure. In all, we have performed forced drainage in twenty-two instances on sixteen patients with nonsuppurative diseases of the central nervous system. The exact method as outlined has been used in sixteen instances on thirteen patients, eleven of whom were suffering from multiple sclerosis. In nearly every instance detailed study of the spinal fluid, cell count, total protein and colloidal gold reaction has been made at frequent intervals throughout the procedure. In eight instances, a complete study of the blood and spinal fluid was made both at the beginning of the procedure (before the pituitary extract was given) and again at the end of the drainage. In these cases, as well as in a larger

9. Kubie (footnote 2, second reference).
10. Kubie (footnote 2, third reference).
11. Kubie, L. S.: Personal communication to the authors.
12. Haldane, J. S., and Priestley, J. G.: J. Physiol. **50**:296, 1916. Priestley, J. G.: Ibid. **50**:304, 1916.
13. Motzfeld, K.: J. Exper. Med. **25**:153, 1917.

group of controls, the following determinations were made in simultaneous samples of blood and spinal fluid at the beginning and at the end of the drainage: osmotic pressure (as measured by the freezing point depression), total protein, nonprotein nitrogen, sugar, total solids, chloride and sodium. These data, together with a description of the methods employed, will be reported in detail separately. It is our purpose to give a few examples, typical of what we have found regularly, to demonstrate that by this procedure both the blood and

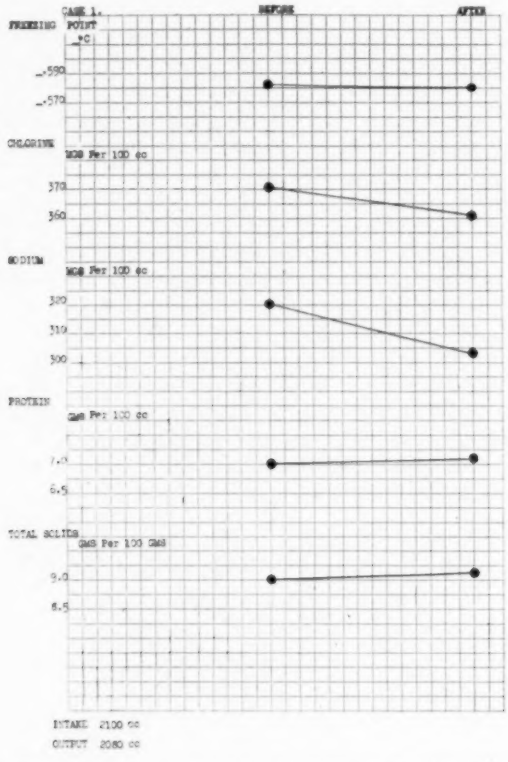

Chart 1.—The changes in the blood serum following the administration of water by mouth, when no pituitary extract is given. The diuresis is prompt and complete. There is no dilution of the serum as a whole. The slight diminution of the sodium and chloride contents is probably due to the sodium chloride lost in the urine. The patient drank 2,100 cc. of water and voided 2,080 cc. of urine during the three hours and twenty-five minutes between the taking of the two samples of blood.

the spinal fluid are rendered hypotonic, a necessary requisite to the theoretical soundness of the method.

When water is taken by mouth in large quantities, prompt diuresis occurs, but little dilution of the blood takes place. This was shown

by Haldane and Priestley [12] and is demonstrated in chart 1. When, however, the water drinking is preceded by an injection of solution of pituitary, the output of urine falls nearly to zero, and the diuresis is delayed from three to six hours or longer. This was first shown by Motzfeld.[13] That a dilution of the blood serum occurs under these circumstances is strikingly shown by chart 2. Here the total osmotic pressure (as shown by the freezing point depression), the total protein, the total solids, the chlorine and the sodium all show dilution. A

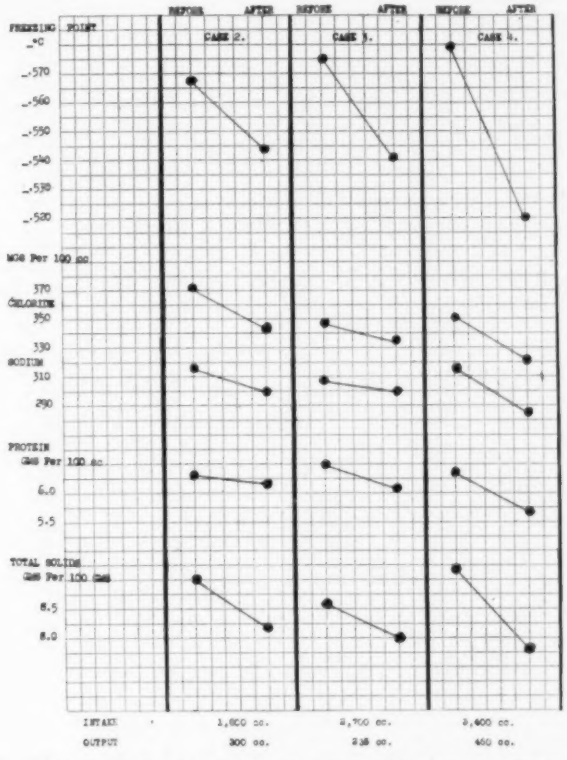

Chart 2.—The dilution of the blood serum in three patients with multiple sclerosis during forced drainage of the central nervous system. Each patient received a subcutaneous injection of solution of pituitary preceding the water drinking. This chart should be contrasted with chart 1. The patient in case 2 drank 1,800 cc. in the four hours and fifty minutes between samples of blood; the one in case 3 drank 2,700 cc. in the three hours and fifteen minutes, while the one in case 4 drank 3,400 cc. in the five hours and forty-five minutes between samples of blood. The output of urine during the procedure was 300 cc. in case 2; 235 cc. in case 3, and 450 cc. in case 4.

There was definite retention of water, as shown by the output of urine. A definite dilution of the blood serum (freezing point, chloride, sodium, total protein and total solids) is shown in every case. A similar dilution of the cerebrospinal fluid is shown in chart 3.

similar dilution is reflected in the cerebrospinal fluid, often after a latent period (chart 3).[14] Charts 2 and 3 are typical of what we have found in every case.

These results demonstrate that human blood serum is rendered hypotonic by our modification of Kubie's method, and that this dilution of the blood is reflected in the cerebrospinal fluid. This clearly indicates diffusion from blood to cerebrospinal fluid under the influence of the procedure. Where that diffusion takes place is not clearly indicated by our experiments, nor have we been able to show that during a given period of drainage, after the administration of solution of pituitary and

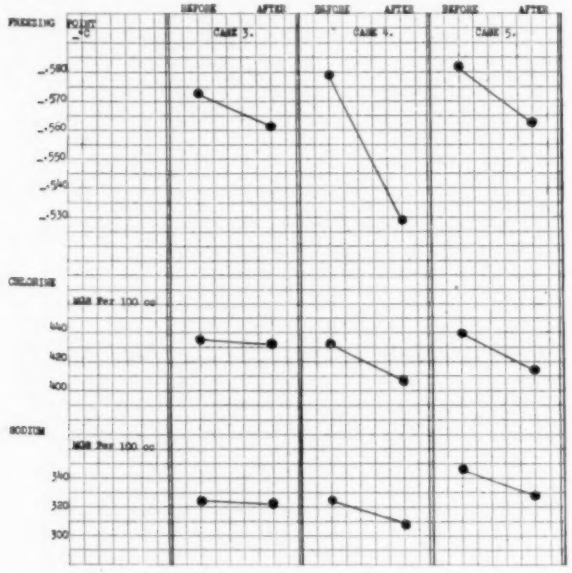

Chart 3.—A dilution of the spinal fluid reflecting the serum dilution shown in chart 2. Cases 3 and 4 in chart 3 are from the same experiments as cases 3 and 4, respectively, on chart 2.

Charts 2 and 3, which are typical of the eight cases in which complete studies of the blood and cerebrospinal fluid were done, demonstrate a definite dilution (hypotonicity) of both blood and cerebrospinal fluid induced by this method of forced drainage of the central nervous system.

water, there is a greater total outflow of spinal fluid than when solution of pituitary is omitted and prompt diuresis is allowed to occur. Even if such an increase were demonstrated, it would not prove that the amount of perivascular fluid pouring into the subarachnoid space had increased.

14. A similar decrease in the calcium and phosphate in the serum and spinal fluid in these cases has been found by Dr. H. Merritt, working in our laboratory. These results will be reported later.

We have no data as to what percentage of the total fluid in the subarachnoid space normally comes from the perivascular spaces, nor any conclusive criteria for judging whether this perivascular increment has been increased or decreased by a given procedure. Kubie [2] has demonstrated, however, as already mentioned, that when the blood is made hypotonic the perivascular and perineural spaces become distended with fluid, while under this identical procedure, but with drainage of the spinal fluid throughout the experiment, these spaces are collapsed. He has also brought forth good evidence to indicate that both in animals and in man cellular exudate (perivascular infiltration) may be forced from the depths of the central nervous system into the

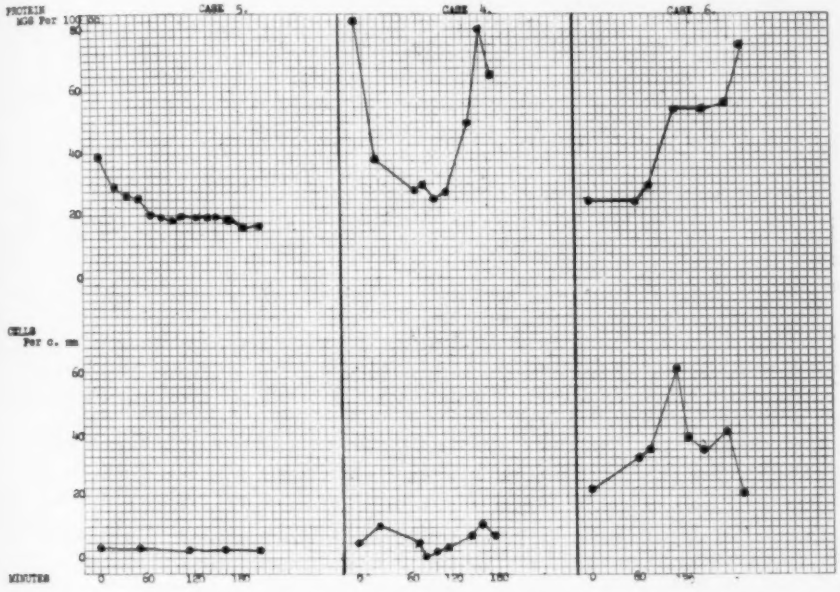

Chart 4.—The remarkable increase in both the protein and the cells of the cerebrospinal fluid (cases 4 and 6) which occasionally occurs during the latter portion of the drainage in cases of multiple sclerosis. Case 5 shows no such increase, the cells remaining unchanged and the protein gradually dropping toward levels approaching that of normal ventricular fluid.

Cases 4 and 6 are consistent with Kubie's idea that perivascular exudate may be drained into the subarachnoid space during such forced drainage of the central nervous system.

subarachnoid space when the latter is drained during the experiment. The fact that in some of our cases the protein content of the spinal fluid in the latter half of the drainage increased (chart 4), and that this increased protein was often accompanied by an increased cell (lymphocyte) count (chart 4) tend to bear out Kubie's contention.

Recent work by Wolff [15] in our laboratory indicates that solution of pituitary has a vasoconstrictor effect on the pial vessels of anesthetized cats.

Further work is in progress and at a later date will be reported in detail. The therapeutic results of this mode of treatment have been sufficiently encouraging to warrant further study. A report of this aspect also will be made at a later date.

CONCLUSIONS

1. When water is taken by mouth after the subcutaneous injection of solution of pituitary, diuresis is delayed and the blood becomes hypotonic.

2. This dilution of the blood is reflected in the spinal fluid after a latent period.

3. A discussion is offered of this modification of Kubie's "forced drainage of the central nervous system."

ABTRACT OF DISCUSSION

Dr. Israel Strauss, New York: When Dr. Fremont-Smith finished his discussion, I found I was in the position of having nothing to discuss, because I cannot see that any one of us here can take exception to the actual facts which he has demonstrated, and also, probably, I think we will have to agree that the spinal fluid is a dialysate. I shall discuss the clinical side of this question and the treatment for multiple sclerosis.

If there is a toxin circulating in the spinal fluid and that fluid is drained for four hours, I cannot see what permanent benefit such a patient is to receive, because one does not know the source of this toxin. No one has as yet proved a toxin to be present in the spinal fluid. Even if it were present and was removed, what good would it do a patient, if one cannot get at the source of the toxin?

Dr. Walter Freeman, Washington, D. C.: What is the origin of these cells in pathologic states? Do they come through the capillary walls? Do they come from those funnel-like areas around the pial surface? Do they come from the perivascular spaces?

If the cells do come from the perivascular spaces, of course, that is a fact of great importance. If they are just forced out of the meshes of the pia, or if they come by diapedesis through the walls of the capillaries of the meninges, it is not of so much importance.

Would it be possible by a study of the cell types obtained in such cases as pernicious anemia, with its fatty granular cells, or in paresis, with its plasma cells, or in the acute meningitides, with their polymorphic nuclei, to determine where these cells come from, whether from the perivascular spaces or merely from the meninges?

Dr. Tracy J. Putnam: I see that we have entered into a large field which we were not particularly anxious to touch on at this time, namely the question of clinical usefulness of this procedure.

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15. Wolff, H. G.: The Cerebral Circulation: XIb. The Action of the Extract of the Posterior Lobe of the Pituitary Gland, Arch. Neurol. & Psychiat. **22**:691 (Oct.) 1929.

We are in no position at present to make any worthwhile report as to the progress with this treatment. In the twenty-four instances in which the treatment has been used in our hands the only ill effect that could possibly be attributed to it is in the case of which Dr. Strauss spoke in which an old man died of bronchopneumonia a week after treatment. We were not convinced it was a result of the treatment.

It would be a great pity if this treatment were announced as a cure of multiple sclerosis and came into general use by the medical profession at the present time.

We have refrained from saying much about the results, except that on the whole they seem encouraging, and we feel that under proper precautions and in the hands of a few who are accustomed to the method and perhaps envisage some of its dangers, it is justifiable to see what more can be done. We are not satisfied with the treatment and would not urge it on any patient but, on the other hand, we know of nothing which is more effective in this disease.

The treatment is somewhat exhausting, but by the use of a special bed which enables the patient to be put in various positions during the drainage, it is not insupportable.

In regard to the etiology of multiple sclerosis, I think we had better say nothing at present, for that matter has already been discussed before the society.

DR. FREMONT-SMITH: So far as I am aware, there is no capillary bed in the meninges. There are arteries, veins, arterioles and venules, but no capillaries. That has perhaps a bearing on the possibility of cells coming through. However, it is also possible that lymphocytes may come through thicker-walled vessels than capillaries.

Dr. Freeman asked a question in regard to identifying cell types, which is well taken. That work lies ahead. Dr. Kubie has clearly pointed the way by his method of vital staining. I should mention that Dr. Kubie, himself, has used this method of forced drainage clinically in the treatment for poliomyelitis and for meningitis. His results will be published in the near future.

I should like to mention one other point which is of interest here. In the work which we have been doing in the past three years, we have been able to show that in the therapeutic fever of typhoid vaccine and of malaria (the studies on malaria were done through the courtesy of Dr. Solomon at the Boston Psychopathic Hospital) there is a situation closely analogous to that which we get when we give a solution of pituitary. That is, water which is drunk is not put out. And we are able to show that it is not just a question of sweating to compensate for it but that there is an actual and marked retention of water in the body. The urine output is almost nil, in spite of the large intake of water. The diuresis is delayed several hours, and a prompt and marked dilution of the blood occurs which is followed by a dilution of the cerebrospinal fluid. We have evidence to show that this mechanism occurs in various acute infections. We would suggest that this has a bearing not only on the clinical picture of meningismus and the results of lumbar puncture in meningismus, but in the clinical improvement that we find in various conditions in which the patients are treated by fever therapy.

TESTS FOR SENSIBILITY

AN INVESTIGATION AMONG NORMAL SUBJECTS*

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This discussion concerns itself with an investigation of tests for sensibility among "normal" persons.

From among the tests originally devised by Henry Head only a few have been selected here for intensive study, and these were arbitrarily chosen because of their wider clinical use and because of their easy applicability. They refer mostly to cortical sensory functions.

For my objective I have set out to determine the number and types of errors that "normal" persons may be prone to make, in order that I might use the observations for purposes of comparison with the results obtained from testing pathologic material.

It will be shown that "normal" subjects make many errors identical with those found in pathologic cases. In this paper the results demonstrate the fact that "interpretation" of pathologic sensory observations is most difficult and always doubtful unless one uses the responses from "normal" subjects as a standard by which the interpretation may be guided.

MATERIAL USED

The material used for this study consisted of 196 normal subjects, ranging in ages from 20 to 76 years. The results in 185 cases are recorded in the accompanying table; the observations in 11 cases were omitted for various reasons. In these subjects none had any demonstrable organic lesions of the nervous system nor any other physical disability which might have interfered with the examinations, so far as could be observed. These subjects represented a mental age the average or better of such patients one may find in the wards of any large general hospital.

TESTS AND METHODS

The tests used were those devised by Henry Head and his co-workers. In some instances the tests have been slightly modified in

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* Read at the Fifty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 28, 1929.

* This paper is one of a series of studies on "normals" from the Graduate School of Medicine, University of Pennsylvania, direction of Dr. T. H. Weisenburg.

technic. The particular ones selected for use in this study were applied because of the limited time in which to work with the available material, together with the easy standardization of such tests, and, lastly, because of their clinical convenience. Most of the tests, because of their convenience, are more widely used in clinical practice, and therefore offer a basis for selection from a practical view. In this investigation only about six subjects were studied per day, the process being most fatiguing and exacting to the examiner. (The work, however, is only a step in the direction of further and more tedious investigations with Head's tests.) The tests and methods of testing may be described somewhat in detail, as follows:

1. *The Appreciation of Shape in Two Dimensions.*—Simple shapes were employed. A circle, square, triangle and an oblong cut out of stiff leather were used; each side of the square, the diameter of the circle and the height of the triangle were 3.5 cm., while the oblong was also of this length and 1.75 cm. in breadth. The subject's gaze was directed away. Each object, separately, was then placed in contact with the palm, and the subject was finally asked to designate the shape of the object. It was found that a cardboard, with the various shapes duplicated in drawing, facilitated the testing by having the subject point to the corresponding shape represented on the cardboard which he believed to be in his palm. Four trials were given with each test, first in one and then in the other palm.

2. *The Appreciation of Size.*—Circular disks of thick leather, increasing by 0.5 cm. in diameter from 1 to 5 cm., were employed in this test. Two objects of different sizes were placed in succession in contact with the palm of the hand, or else two objects of the same size were used. The subject was requested to look away and then asked to distinguish which was the larger, if either, of the two objects. Four trials were given with each test, first in one and then in the other palm.

3. *The Recognition of the Position of the Forefinger and Great Toe When Passively Moved.*—There were four trials given with each position of the toe or forefinger—down, up or straight. In each case the toe or forefinger was grasped in either of two ways: (1) by the examiner's thumb and index finger resting over the nail and below the ball of the member, and (2) by the examiner's thumb and index finger resting on either side of the subject's toe or finger.

4. *The Appreciation of Difference in Texture.*—For this test a set of common materials was employed, viz., silk, wool, linen and velvet. With his gaze directed away each subject was allowed to palpate or finger the various stuffs one at a time and in each hand separately. As he did this each piece of material was identified by name for him. Then, with his gaze still directed away, he was given identical stuffs to finger in each hand, or else dissimilar materials, until all the combinations had been exhausted. He was finally asked to state whether the cloth in each hand was alike or different, to state how they were alike or different and if possible to identify them by name.

5. *The Recognition of Common Objects.*—With the subject keeping his eyes closed, various objects were successively placed in his hand to finger, and he was then asked to name, in turn, the following: pencil, door key, Yale key, comb, matchbox, knife, screw-driver, paper clip, safety-pin, piece of rubber hose, spool and coins—penny, quarter and nickel.

RESULTS

The results of the investigation have been tabulated numerically as to the following: the number of cases studied in each age decade, the number of errors found with each portion of the several tests and lastly the total percentage or errors for the entire group with each portion of the various tests.

TEST 1.—The type of errors is fairly uniform. Most of the subjects recognized the circle easily. A square was often interpreted by the

Results of Investigation of Various Tests in 185 Cases

Ages	20-30	30-40	40-50	50-60	60-70	70+	Total Errors	
Number of cases	38	35	35	56	18	3	No.	Per Cent
Recognition of Shape; Two Dimensions								
Square	4	2	5	8	2	0	21	11.0
Triangle	4	7	5	5	2	0	23	12.0
Oblong	7	6	4	8	3	0	28	15.0
Circle	2	1	1	2	0	0	6	3.0
Recognition of Size								
½	15	18	12	21	2	2	70	34.0
1	3	0	1	2	0	0	6	3.0
2	0	0	0	0	0	0	0	0.0
3	1	0	0	0	0	0	1	0.5
Equal	27	20	26	38	14	3	128	69.0
Recognition of Passive Movements; Toe and Finger								
Great toe								
Down	1	0	0	0	0	0	1	0.5
Up	0	0	0	0	0	0	0	0.0
Straight	1	0	0	0	0	0	1	0.5
Forefinger								
Down	0	1	0	0	0	0	1	0.5
Up	0	2	0	0	0	0	2	1.0
Straight	0	2	1	0	0	0	3	1.6
Recognition of Similarity and Difference in Textures								
Wool	7	3	5	10	0	0	25	13.0
Silk	9	4	8	10	4	0	35	19.0
Linen	8	2	8	17	6	0	41	22.0
Velvet	0	0	2	8	2	0	12	6.0
Linen-velvet	2	0	0	0	0	0	2	1.0
Wool-velvet	3	3	2	1	2	0	11	6.0
Silk-velvet	6	0	0	0	0	0	6	3.0
Linen-wool	2	2	2	9	2	0	17	9.0
Linen-silk	0	1	6	3	1	0	11	6.0
Silk-wool	0	0	0	2	0	0	2	1.0
Recognition of Common Objects *								
Penny	8	2	1	2	9	3	25	13.0
Nickel	3	2	3	2	8	1	19	10.0
Quarter	8	1	1	1	3	3	17	9.0

* All other common objects were recognized by all.

subject as an oblong or triangle, an oblong as a square or triangle and the triangle as a square or oblong. A circle was rarely confused with the other shapes. A cardboard, as described, is absolutely indispensable with the average run of subjects. They showed a great degree of uncertainty in identifying an object by name without the cardboard.

TEST 2.—The greatest percentage of errors occurs between two disks of equal sizes in the second test. The only explanation for this can be an obvious psychologic one. Between disks varying only 0.5 cm. in size, the next largest number of errors occurred. A partial

explanation of the resulting errors may be accounted for in the methods used in testing; when a disk 4.5 cm. in diameter was followed by one 5 cm., the subjects showed a marked tendency to call them of equal sizes. In changing from a disk of 5 cm. in diameter to one of 4.5 cm., however, the subjects more often correctly called the difference. Peculiarly, this type of mistake does not seem to occur in nearly the same proportions with any other two disks which vary only 0.5 cm. in size.

TEST 3.—Either method of grasping the toe or forefinger resulted in a correct response from practically all. It seems best not to suggest to the subject that his toe is up when it is really down or straight, or down when it is up or straight, etc. Errors because of a subject's suggestibility are merely guesswork. No such mistakes were recorded in this tabulation.

TEST 4.—Every one of the normal subjects recognized all of the common objects except when coins were used. They failed to identify the denomination of the coins correctly, although they could identify the objects as coins.

TEST 5.—The results of the test for the appreciation of difference in textures was found, on analysis, to be the most interesting of all those obtained. Before discussing this test further, it will be well to note what Head [1] stated with regard to its significance:

> The power of recognizing various stuffs by feeling them with the fingers is obviously dependent on the accuracy of tactile impressions. But there is another aspect of this test, which demands the same faculty of appreciating essential similarity and difference underlying the recognition of weight and form. This appeal to two sides of the cortical activity can be demonstrated by choosing cases of sensory dissociation—if tactile sensibility is perfect, whilst the tests and various weights and shapes are manifestly affected, the power of recognizing stuffs by their texture will be disturbed in one direction; another sort of defect is found where touch is impaired, and weight and shape can be appreciated without fail.
>
> No. 16 was a characteristic example of the first condition, the more striking because the whole hand exhibited this form of dissociation. Here, then, was none of the difficulty so often experienced when some fingers are affected and others are not; the various stuffs could be frankly placed in his hands, and he could feel them freely in a natural manner. The index and little fingers of the two hands responded to a hair of 14 grm./mm.^{2}, and the palms to one of 21 grm./mm.^{2}, showing that tactile sensibility was in no way defective. He was allowed to take each of the following stuffs into his affected hand and to palpate it as he might desire. It was then transferred to the normal hand. Flannel in the left (affected) hand was said to be "something rough," but was recognized at once on the other side. Silk was said to be "smooth, silky," but was called silk in the normal hand; corded velvet and cotton were thought to be "something

1. Head, Henry: Studies in Neurology, London, Oxford University Press, 1920.

rough" on the affected side, though recognized as "corded stuff" and "cotton" over the normal parts. When a piece of corded velvet was placed in the two hands at the same time, he said: "They are quite different stuff. The piece in the right hand is corded; it feels rougher and thicker. The piece in the left (affected) hand seems smoother and more like calico; I don't think it is silk."

It was not, however, the smoothness and roughness that were not appreciated, but the essential difference which enables us to give each textile material its specific name. It was, in fact, an "agnosia." This view is borne out by the character of his answers to the tests for the recognition of form and of common objects. In every case, with wooden blocks in the left (affected) hand, he said, "I don't know," though they were perfectly recognized on the normal side. He had no difficulty in naming correctly a knife, penny, sixpence, and scissors in the right palm, but said, "I don't know," when the same objects were placed in the left.

Further on, in referring to patients of the second class, Head said:

Patients, in whom the loss of recognition of textures belongs to this class and is associated with a want of tactile sensibility, usually attempt to name the stuff placed in their hands; but they frequently add some explanation of the difficulty they recognize in determining the character of the material. They say, for instance, "That is cotton, I think, but I can't feel it so well as in the other hand." "I can always feel the silk, but it is with the rougher materials that I have difficulty."

Head concluded:

In the one case, the patient's answers approximate to "I don't know what it is," whilst in the other he has a greater tendency to hesitate and to be puzzled by the curious sensory differences in the two hands; generally, however, he makes a guess, which would be recorded as a normal response were it not for the explanation with which it is so frequently qualified.

The results of this study throw a different light on the test for the appreciation of difference and similarity of textures. A striking percentage of errors occurred. In a typical error, the subject, when allowed to finger identical stuffs in each hand, replies: "They are not alike, I'm not very good at telling these, but the one in the right hand is smoother, it's a little finer too. In this hand (left) it is heavier and rougher. No! they're not alike." With other identical pieces the same subject is apt to reply that the stuff in the left hand is smoother and finer and that in the right hand heavier and rougher.

Other subjects will deliberate a few minutes while reading into their appreciation of similarity and difference all sorts of different qualities. This is particularly so of the older age groups. Finally, they will often conclude that the stuffs "are the same, but certainly they are of different quality." This is a frequent mistake. No errors of this sort, however, were tabulated. Only those errors of a gross sort were recorded, for instance, when two pieces of silk were given and one was said to be silk and the other an entirely different stuff.

A barber and a textile worker made perfect scores in all the tests. With textures, the former remarked: "In my business I am used to using the tips of my fingers and have a well developed feeling in them." And in the case of the latter: "It's my job to sort out materials and I could tell with my eyes closed the differences in various grades of woolen." Some made perfect scores in all the tests except textures. Others erred in a few of the other tests but accomplished perfect results with the stuffs.

Among the various stuffs those of similar materials offered the greatest difficulty; silk and linen were more difficult to recognize as such than either wool or velvet. The percentage of errors with dissimilar stuffs was decidedly less than with identical stuffs.

COMMENT

Some of the causes for errors have already been indicated under the description of the results for each of the various tests. They are due to the methods or "technic" of testing, such, for example, as the use of the two larger disks in the test for the appreciation of size.

The test for the appreciation of similarity and difference in textures is interesting from two views with regard to Head's remarks about its significance. If such gross mistakes as these subjects made depend on an impaired tactile sensibility, then it is logical to assume that a great many normal persons have an impaired tactile sensibility in their fingers. This is possible, although it would have to be demonstrated by the use of von Frey hairs before being actually proved. Still, one can hardly believe that so large a percentage of normal subjects as shown by this investigation have some impairment of tactile sensibility. If they do, the test then becomes of decidedly less clinical value because of the necessity for the use of von Frey hairs, which involve a tremendous amount of work. If, on the other hand, the results depend on either the intactness or the loss of cortical function, then the high percentage of errors indicates that the test again is doubtfully dependable as a clinical method for testing the appreciation of similarity and difference in textures. Not all of the errors resulting from this test can be accounted for on the basis of a lack of attention or concentration on the part of the subject. When the attention was excellent, there resulted errors with identical stuffs but not with dissimilar textures.

A few brief remarks will serve to give an explanation for the majority of mistakes encountered with these particular tests. Attention and concentration on the part of the subject outwardly may appear to the examiner as good, but when mistakes are encountered persistently it may be well merely to ask the subject if he is attending. The reply accounts for many errors. At other times when the subject may affirm that he is attending, it is obvious to the examiner that he is not attending.

Physical discomforts, such as a full urinary bladder, an uncomfortable feeling of peristalsis, a slight headache about which the subject so minimizes as not to mention it and other similar factors, greatly interfere with the subject's attending. When mistakes are repeatedly encountered in the same subject, it becomes necessary to enquire as to any physical discomfort he may have. In some cases the subject may feel apprehensive of what the tests are about; perhaps he may feel that it is some form of mental testing, and that he will be shown up. There are those who constantly apologize for mistakes they anticipate and are therefore apt to become confused and resort to guessing. Some are embarrassed because of a soiled garment they may have been wearing at the time, or because of an untidy personal appearance, and cannot concentrate well on account of the embarrassment they feel. In all such cases the examiner should discontinue the testing until the subject is put at ease. In the beginning of each test errors will occur, and it will be necessary that he clearly understands what is wanted of him. It is best that the examiner refrain from indicating his own feeling as to how the results are going with each individual subject. Nothing so interferes with the results as when the examiner indicates that he is vexed with the subject's ability to attend. The examiner, too, must be honest with himself and not charge off a mistake to the subject when it really is the fault of the former.

Criticism has been leveled at Head's tests and methods of testing from a practical view, and justly so; it is almost impossible in a hospital ward to study a case with the same serenity of environment that Head found to be most conducive to his results. Yet, the very same tests which were used in this investigation can be applied in a busy hospital ward provided one discounts the errors which normal persons make from lack of attention from any cause. The texture test, however, is not so easily explained away, for there are subjects in whom the errors cannot be based on any lack of attention or concentration or on any technic peculiar to the test. Possibly some "normal" subjects have never learned to discriminate textures by the sense of touch.

The more complex psychologic aspects of "touch" sensation with regard to textures have not been undertaken in this investigation. They afford a special study in themselves. It was interesting to note, however, that throughout the investigation the "softness" of velvet afforded a pleasant "touch" sensation to the majority of subjects.

SUMMARY

1. A study of "normal" persons was undertaken in order to determine the number and types of errors these subjects made—as compared with the errors "pathologic" subjects make—when tested for various types of sensibility.

2. Certain of Head's tests were selected for the investigation because of their wider clinical use and because of their comparatively easy applicability. They appeal mostly to the cortical sensory function. These tests are: the appreciation of shape in two dimensions, the appreciation of size, the recognition of the position of the forefinger and great toe when passively moved, the appreciation of the differences in texture and the recognition of common objects.

3. Approximately 200 adult male subjects, ranging in age from 20 to 76 years, were studied. They had no demonstrable organic disturbance of the nervous system or any other apparent physical infirmity which might have cause to interfere with the testing. The mentality of these subjects was at least equal to that of a similar group of patients in the wards of any large charitable hospital.

4. The results of the investigation confirm those of Head in respect to the necessity for the cooperative attention and concentration on the part of the subject tested. It is necessary that the examiner attend equally well. The results differ from those of Head in respect to certain portions of the tests for "size," "shape," and "textures." A little over one fifth of all the subjects examined failed on disks which varied only 0.5 cm. in diameter. Part of the failures may be attributed to the methods of testing when the two largest disks were used. Most subjects were highly suggestible when disks of equal size were employed. Mistakes in "shape" would have mounted tremendously had a cardboard not been used with this test; many of the subjects became confused in identifying "shapes" by name. A rather high percentage of the subjects failed with identical pieces of silk and linen, less with wool and still fewer with velvet; dissimilar stuffs caused little difficulty. Practically all did very well in recognizing the positions of the forefinger and great toe when passively moved; here again the subjects were found to be somewhat suggestible.

Excepting coins, common objects were recognized uniformly well by all the subjects tested. Although coins were recognized as such, difficulty was encountered in identifying the denominations by a high percentage of the subjects.

CONCLUSIONS

Results of the investigation of tests for sensibility among "normal" subjects warrant the following conclusions:

1. "Normal" subjects make many errors identical with those obtained in testing "pathologic" sensory material.

2. Many subjects are suggestible, and it is best that the examiner refrain from confusing his subjects should good results be obtained.

3. The reason for the mistakes made by "normal" subjects may be attributed in part to the tests and methods themselves, but largely

to lack of attention and concentration on the part of both the subject tested and the examiner.

4. In the test for the appreciation of similarity and difference in textures, the high percentage of errors encountered with identical pieces of silk and linen—wool and velvet to a lesser extent—is difficult to explain away entirely on the basis of a lack of attention and concentration. Some subjects may never have learned to use the sense of touch where the finer qualities of stuffs are concerned. (Further investigations need to be done with this test.)

5. Lastly, it is believed that these tests may be used in an ordinary hospital examining room with good results, and that the interpretation of the observations may be greatly facilitated, provided one has an appreciation of what the "normal" subject does under similar circumstances of testing.

ABSTRACT OF DISCUSSION

DR. S. E. JELLIFFE, New York: I shall attempt to bring your recollections back to the beginnings of medicine, and shall attempt a Hippocratic quotation, but not in the original: "Art is long. Life is short. And experience is fallacious."

The father of medicine has confirmed what our Philadelphia confrères have just presented to us, and I was compelled, as I read the paper antecedent to hearing it, to note the quotation marks around the word "normal." This is a clear indication that they themselves were somewhat doubtful as to what "normal" really meant, and further, if I may go back again to the same Greek fathers, they also had something of value to say about the question of normal.

Previous to Plato, there seemed to have been some relativists, but, with Plato, the absolutists came into the chair, and since Plato's day there have always been plenty of fundamentalists, who always know what "normals" are. The mental tic of always knowing about everything began then. Whether it was due to a difficulty in the antrum or whether it had something to do with the mycotic infections of the foot, which are so prevalent, I do not know. At any rate, the mental tic of normal persons started early, and I am delighted to see this onslaught on it even at this late date.

One point which also was not lost to the early Sophists was the difficulty of permitting the coming to consciousness of symbolic representations of sensory stimuli on the basis of affective identifications. It seems to me that the paper presented illustrated this very well, so far as statistics are concerned, but did not enter into the question as to the reasons thereof.

Many of the false answers in so-called normal persons are due to affective identifications with their accompanying emotional resistance. There results therefrom faulty discrimination. The point is well taken how necessary it is in making such sensory tests to exclude any possibility for suggestive or other type of disturbing factors capable of bringing about affective situations as emphasized. This is an important situation in all tests of this sort.

That situation is directly related to this one because, as has been emphasized here, the barber, for instance, the tailor or the worker who in his ordinary avocation is called on to utilize certain sensory discriminative capacities, develops a type of response reaction different from that in another avocation.

So I congratulate the Association on this return to Hippocratic medicine so ably presented by our Philadelphia confrères.

DR. FREEMAN: As regards these normal tests. Do the two hands show any significant differences? We are so predominantly a right-handed race that it would be interesting to know whether or not the threshhold for the recognition of these various stimuli is different on the two sides.

In testing a patient for disturbance of sensibility, our judgment of the normal is dependent not on the abstract, a previously set-up idea of what the normal should be, but on the concrete example of the opposite hand. Of course, when both hands are involved, we are in some difficulty and we have to draw on our knowledge of the abstract normal, but when we are testing for slight diminution in the aspects of sensibility, we use the opposite hand for our normal, and this, of course, can fluctuate.

In regard to the normal, I shall also introduce a mathematical term of the median: it is the point at which the greatest number of cases occur. There can be many above and many below, but the greatest number of cases occurred at the median.

DR. ERNEST SACHS, St. Louis: I have found that the application of the sensory tests of Henry Head are often difficult, and I ask Dr. LaMar and Dr. Weisenburg whether or not they have made use of the idea which I think has been mentioned in Henry Head's work; for instance, in testing the texture of objects, are the objects first given to the patient to feel before he is blindfolded and asked to test them?

It has been everyone's experience with pathologic cases that unless a person knows what the tests are going to be beforehand, he is liable to make a much larger number of errors.

DR. WEISENBURG: About four years ago our group began the study of normal persons. In our first study of the current methods of testing for aphasia with particular attention to Head tests, we found that normal subjects made the same percentage of errors and the same kind of errors as pathologic subjects.

In our second study on sensation, Dr. Pearson showed that vibratory sensation is gradually diminished, in the lower limbs, decade by decade, after the fiftieth year.

From that time on the scope of our investigation of normal persons has increased. Dr. Kubitschek has just finished a year's work in the study of the secondary sex characteristics in the male. He studied about 600 cases, using normal persons of from 10 to 18 years of age. Another of our students, Dr. Anderson, has finished a year's work on the problem of enuresis, and Dr. B. J. Alpers, a thesis on the development of speech in children. Two of our students, Dr. Waggoner and Dr. Ferguson, are studying the development of the Babinski reflex in infants by means of moving pictures.

We have now in contemplation further work on the testing of aphasia, sensation and allied topics.

The work of Dr. LaMar shows rather decisively that one cannot depend on the ordinary tests for sensation which neurologists usually employ. We have come to the conclusion that we cannot depend on our present methods of clinical testing, for there is such a large variation in normal persons that unless one knows what these variations are the testing of pathologic subjects must be fallacious.

DR. F. TILNEY, New York: I cannot help but feel that such a thing as a normal person is a most unusual product of our species. The variations in every particular are so wide that it seems difficult to establish any average standard that might be entitled to be called a normal. We all depart in so many ways from such theoretical standards that it seems unwise and perhaps unsafe to think of such a thing as a norm. What is normal for one person and may make that

person adaptable to a certain environment would not be considered so in another person under different circumstances.

So that for us, as neurologists, who are endeavoring to have a concept such as we may call a standard in order to gage our work and know when we are dealing with distinctly pathologic conditions, it is, to my mind, a difficult undertaking, and is what Dr. Weisenburg has shown in his work on sensation, aphasia or speech defect, speech organization, and all other particulars in which he has made an approach to the so-called normal standard. In the matter of sensation particularly I feel that it is most difficult to be sure when one is dealing with an actual pathologic condition.

Several years ago, G. Stanley Hall, in a study of Laura Bridgman, the deaf, dumb and blind woman, who was such a profitable subject of study in her day, came to the conclusion that this particular person had a two point discrimination on the fingers and on the tongue which was two or three times as acute as the average. That is about the way G. Stanley Hall stated the fact. Subsequently, in studying Helen Keller, I found that she had exactly the same degree of acuity and two point discrimination which Hall attributed to Laura Bridgman. In fact, I was surprised to find that several blind girls whom I examined had an even keener sense of two point discrimination than Laura Bridgman was said to have and than Helen Keller possesses.

So that as between these statements of a refinement in sensation, illustrated by these two excellent examples, it is difficult to judge. Furthermore, so much of sensation is highly conditioned by the training of the person. That applies not only to the 2 point discrimination, but to localization; it applies equally to pressure sense, and I believe even, to a lesser extent, to the vibratory sense.

In the matter of sensation, then, particularly in its higher syntheses, I am sure that it is going to be most difficult to establish anything that approaches a normal standard because behind the sensory equipment is the person's intellectual attainment and training, that is, the condition, and it is not surprising to find, as Dr. Weisenburg and his group have found, that in such a matter as stereognosis the widest range of variability exists, and that persons who apparently should be able to have stereognostic perception easily are often at fault, and those who are especially trained in certain details of sensory perception far surpass what seems to be the upper normal average.

I think, however, that the work that has been undertaken by the Philadelphia School gives, in its present statement, promise of real achievement for the future, and that it will put in our possession a series of observations and actual measurable facts which will give a much clearer understanding of what we may expect when we come to examine any given case. And I think that a great many of the things we now consider outside the limits of the normal we will have to accept later on as well within that range.

So whether or not an actual norm for sensation, speech, reflexes, motor control or any other detail of neurologic organization is ever established, we shall have the low and the high limit within which to expect normal variation. On this basis, we shall be in a position to evaluate the clinical manifestations as they present themselves better than we have heretofore.

Dr. A. Meyer, Baltimore: This discussion refers to something which illustrates clearly some things that were discussed in connection with our evaluation and treatment of the structural and the functional facts concerning man.

It is obvious that we cannot be neurologists only in the sense that we think we can test the functioning of the sense organs as such. As soon as we take up the study of the sensibilities, and not only the reflex reactions but the patient's

account, we immediately introduce the psychobiologic aspects of reaction, and we have to know what we do when we handle that. We have there a wide range of relativity and, therefore, not the same ease of assuming that such and such a thing must be normal. We have a duty to determine the range of the reactivity of the individual and the dependability of the results for certain purposes.

In studying the methods of examination for sensibility, we have to learn to apply a principle of economy because one of the great difficulties in this whole field comes from the fact that too many things are tried and often they are not particularly well focused to do the main thing, namely, to bring out the reactions which would have definite reference to certain neurologic issues that we want to discriminate. The range of possible psychobiologic reactions to outside stimuli is so great that we have to focus, and, therefore, the physician has to know how to get the minimum number of issues tried in as dependable a way as possible, so as to make sure that we have definite reference to the issues that we want to differentiate. Therefore, the importance of knowing what sort of reactions we consider differential throws a light on the structural and functional operation on the sensory side.

I think that the question of economy in this large mass of psychobiologic material that we can elicit and the determination of finding where it points definitely to the issues that we want to discriminate are far more important than any discussion of what is normal or not normal. I think that the study undertaken along these lines is exceedingly interesting and it is just this sort of facts that I consider one of the best examples of what I understand by consideration of the psychobiologic functions and aspects of man.

DR. N. C. LAMAR: I was pleased to hear Dr. Jelliffe further emphasize the affective factors surrounding and entering into the sensory testing.

Regarding the differences we might have found in the two hands with some of our tests, at first we found some difference with regard to the hands of the individual, but later we always asked the subject whether he was right or left-handed and if he was right-handed we always gave him the test in the right hand first. If, in a right-handed person, the test is made in the left hand first, the subject is apt to feel a little resistant toward the testing. He feels that he is not, perhaps, getting off on the right foot, so to speak.

Regarding the textures, in each case we gave the subject the material to finger beforehand, with his eyes closed. He was allowed to finger it as long as he wanted to, feeling it carefully, and it was then identified by name for him before the tests were given.

MYELORADICULITIS

A CLINICAL SYNDROME, WITH REPORT OF SEVEN CASES *

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We recently observed a series of patients of unusual interest. They uniformly presented rapid development of motor and sensory signs with kaleidoscopic improvement or recovery. There was involvement of the motor and sensory components, at times in the nerve roots, at other times in the spinal cord substance, and in some of the cases in both the nerve roots and the cord. The similarity between all these cases led us to the opinion that there is a common etiologic agent. That this may be an infectious agent is probable, for in almost all of the cases the patients gave a history of a preceding inflammation of the upper respiratory tract. Ordinarily, each case taken by itself could have and probably would have been designated as an infective myelitis, and individually would perhaps have created no special interest. None of the cases can properly be labeled as purely neuritic. The rapidity of improvement and the persistent involvement of the nerve roots with minimum disturbance of the cord take this group out of the usual clinical entity designated as myelitis. We present them, then, as an unusual series involving the nerve roots and cord and propose the term myeloradiculitis as a designation for the clinical syndrome.

A study of the literature does not reveal any identically similar group. Instances of myelitic and neuritic disorders from various infective agents are numerous. Thus Cushman, in 1886, reported typhoid fever as the cause of acute ascending myelitis and demonstrated the presence of *Bacterium typhosus* in the cord. Hatori and Shojii [1] described an epidemic of polyneuritis following a disease the clinical course of which simulated influenza. Powers [2] reported a case of postdiphtheritic myelitis. A possible relationship between neuritis and epidemic encephalitis was discussed by Lillienstein,[3] and Sharnke and

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* From the Neurologic Service, Mount Sinai Hospital.

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1. Hatori, J., and Shojii, T.: China M. J. **31**:347, 1917.

2. Powers, H.: Boston M. & S. J. **184**:45 (Jan. 12) 1922.

3. Lillienstein: Ztschr. f. d. ges. Neurol. u. Psychiat. **5**:84, 1923.

Moog [4] reported twelve similar cases. Barker, Cross and Irwin [5] discussed extensively a group which they designated as meningo-encephalomyeloneuritis. Bassoe,[6] in 1920, described several cases showing meningoradicular involvement and postulated their etiology as encephalitis. In 1924, in another communication, he added that the patient in one of these cases had developed a parkinsonian syndrome. Margulies [7] also reported a series termed by him myeloradiculopolyneuritis in epidemic encephalitis. His patients, however, though they to some extent resemble those in our cases, showed in addition hyperkinetic phenomena. Kennedy's [8] conception of infective neuronitis does not apply to any of our cases. His cases, and also those described by Casamajor [9] and Bradford, Bashford, and Wilson [10] were of a more fulminating type, and usually terminated fatally. Every one of our patients recovered. Series of cases have also been reported by Guillain, Barré and Strohl,[11] Francois, Zuccoli and Montus,[12] and Bériel and Devic.[13] These all seem to show maximum invasion of the peripheral neural components. Organic sphincter involvement was usually present, however, and this, together with the finding of changes in the spinal fluid, suggest to some extent our group. All of our cases were observed during the year 1916. It is possible that the various other groups described, viewed together with our cases, represent an epidemic neural invader, with varying degrees of virulence at different periods.

REPORT OF CASES

CASE 1.—A. B., a salesman, aged 27, was admitted to the neurologic service on June 8, 1926, complaining of difficulty in walking of six hours' duration. The onset was sudden, with pain in the back, but it was not of sufficient severity to cause him any concern. He boarded a bus, and after a short ride attempted to arise. There then occurred a violent stabbing pain in the region where the milder pain had been. With the aid of other passengers he attempted to walk, but the pain then radiated down both lower extremities to the popliteal region.

4. Sharnke and Moog: Ztschr. f. d. ges. Neurol. u. Psychiat. **5**:90, 1924.

5. Barker; Cross, and Irwin: Am. J. M. Sc. **159**:157 (Feb.) 1920.

6. Bassoe, P.: Delirious and Meningoradicular Types of Epidemic Encephalitis, J. A. M. A. **74**:1009 (April 10) 1920.

7. Margulies: Deutsche Ztschr. f. Nervenh. **89**:262, 1926.

8. Kennedy, Foster: Infective Neuronitis, Arch. Neurol. & Psychiat. **2**:621 (Oct.) 1919.

9. Casamajor, Louis: Paralysis Among Troops, Arch. Neurol. & Psychiat. **2**:605 (Dec.) 1919.

10. Bradford; Bashford, and Wilson: Quart. J. M. **12**:88 (Oct.) 1918, (Jan.) 1919.

11. Guillain; Barré, and Strohl: Bull. et mém. Soc. méd. d. hôp. de Paris **40**:1462, 1916.

12. Francois; Zuccoli and Montus: Rev. neurol. **36**:95 (Jan.) 1929.

13. Bériel and Devic: Presse méd. **33**:1441 (Oct. 31) 1925.

He then became suddenly "weak in the knees" and could not walk. He managed to return home, however, but the pain became so intense that he was rushed to the hospital.

On admission, he appeared acutely ill and in great pain. There was marked motor weakness in all the muscle groups of both legs and thighs. The knee and ankle jerks were diminished, but the abdominal reflexes were active. A zone of hyperalgesia from the second to the fifth sacral segments was present. There was difficulty in starting the urinary stream. He was admitted to the hospital at 12:30 a. m. When he was seen again on the morning rounds at 9 o'clock there was scarcely any remaining motor weakness, and the zone of

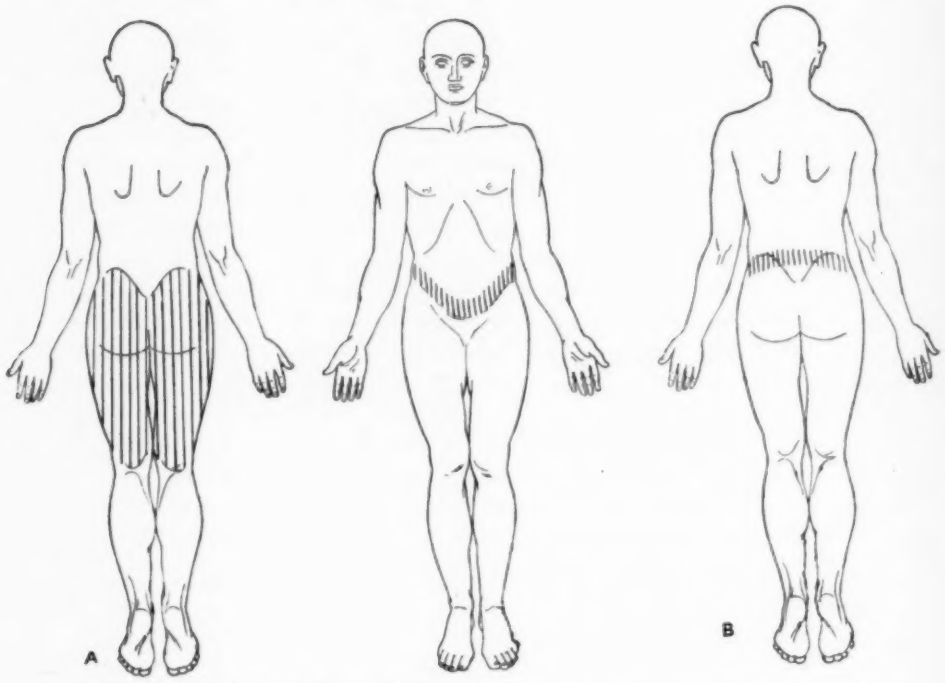

Chart 1 (case 1).—Sensory chart of A. B. *A*, sensory examination on admission, revealing hyperalgesia from the second to the fifth sacral segments. *B*, sensory examination on the physician's general rounds the morning after admission, showing belt of hyperalgesia at the twelfth dorsal segment with mild diminution below this level. There was no motor impairment at this time, but there was improvement in sphincter control.

hyperalgesia had been replaced by a level at the twelfth dorsal segment below which there was diminution of pain, temperature and tactile sensation (chart 1). The difficulty in starting the urinary stream persisted until the following day. Lumbar puncture on June 9 revealed a clear fluid, no pleocytosis and no evidence of block. The Wassermann reactions of the blood and spinal fluid were negative. Improvement was rapid, and when he was seen again on October 8, four months later, in the follow-up clinic, a complete neurologic examination revealed no objective or subjective evidences of any structural disturbance.

Comment.—If it were not for the definite motor and sensory changes found on admission and the organic sphincteric disturbance, this patient could well have been considered as suffering from a functional condition. The character and radiation of the pain at the onset indicated disease of the nerve roots. The presence, however, of the impaired bladder control and sensory disturbances indicates that there was at least mild involvement of the cord. Within nine hours of admission and eighteen hours after the onset of symptoms, he was practically well. An illness that started acutely as if about to invade the cord and produce a severe myelitis had passed off and had limited its maximum insult to the nerve roots.

CASE 2.—E. W., a music writer, aged 37, admitted to the service on April 2, 1926, twelve days prior to admission caught "cold." He was in bed two or three days with rhinitis, cough and some fever. On getting out of bed on the fourth day, he took a long walk and that night noticed that the skin over the chest, back and arms felt irritated, and that these parts were painful and sore. The next day he was worse and was sure that he had grip. Later that day, he perceived "pins and needles" sensations in the legs. Two days later, there was difficulty in voiding, and the next day retention, requiring catheterization. At the same time, marked obstipation developed. The following day the legs suddenly felt numb and weak, and it was necessary to assist him in getting about. He went to bed and though at first able to move about in bed soon found himself totally paraplegic, and the legs felt frozen and dead. At this time a sensation of a belt being drawn about the lower ribs was noted.

On admission, he appeared toxic, pale and wan. He was extremely apprehensive. The positive observations were a complete flaccid paraplegia with nonelicitable abdominal, cremasteric, knee and ankle reflexes. There was anesthesia below the tenth dorsal segment. Between the eighth and the tenth dorsal segments there was a zone of hyperalgesia. Position sense was lost at the toes, but vibratory sensation was preserved (chart 2). Lumbar puncture, done on April 4, 1926, revealed clear fluid under normal pressure and 27 lymphocytes per cubic millimeter. He was immediately started on a course of intravenous typhoid vaccine therapy and made slow but steady improvement, in motor as well as in sensory function. Within a week, bladder function had returned. On April 20, he developed signs of urethritis and prostatitis which proved to be of *Bacillus coli* origin. For a week he had a fever (from 103 to 104 F.). Under systematic treatment this subsided, and he then went on to an uneventful convalescence. When he was discharged on May 28, the only observation in the neurologic status was a mild weakness in the calf muscles of both legs. He was seen again in the follow-up clinic on June 30, 1926, and was entirely well. The only vestige of the illness was some diminution in the deep reflexes.

Comment.—The path of invasion in this patient may be visualized. There was first an inflammatory process in the upper respiratory tract. Then occurred the pain in the back and chest of radicular origin. The organic sphincter disturbance then indicated actual involvement of the cord; which became intensified, as evidenced by the paraplegia that ensued. The disease process, then, started from without and invaded first the roots and then the cord substance. The urethral infection was coincidental.

CASE 3.—A. F., a housewife, aged 56, was admitted to the service on May 25, 1926, complaining of weakness in both upper extremities. Eight weeks prior to admission, she had a severe "cold" with coryza, conjunctivitis, fever, etc. Three days later, she awoke in the morning with severe pain over both lower extremities radiating up and down the arms and forearms. She then felt as though the arms were "dying away" and shortly thereafter could not raise the involved limbs. No movement of any kind was possible in the right arm, forearm, hand or fingers, nor in the muscles of the left arm or shoulder. For the following two months this state of affairs persisted, except for some mild improvement in motor power of the right hand, and ability to raise the left upper extremity slightly. At no time were there any other symptoms.

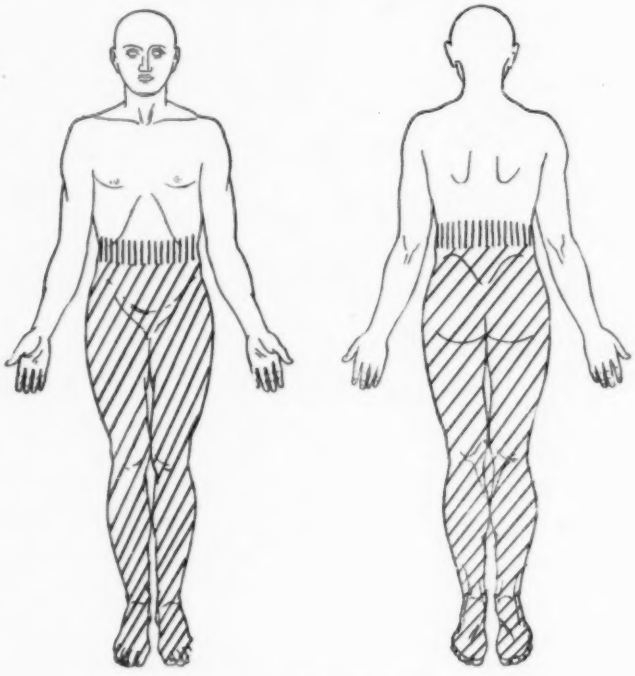

Chart 2 (case 2).—Sensory chart of E. W.

On admission, the positive observations were paralysis of the interossei, biceps, pectoral, and deltoid muscles on the right side, with marked paresis of the flexors and extensors on that side, and less marked weakness in the supinators and pronators of the forearm and of the triceps. On the left side, the same muscles were involved, with the exception that there was somewhat more power in the triceps muscle. There was distinct atrophy of the deltoid and suprascapular muscles. The upper deep reflexes were all markedly diminished, and the biceps reflexes could not be elicited. There was hypalgesia, thermhypesthesia, and hypesthesia in the distribution of the fourth cervical to the fourth dorsal segments (chart 3). Examination of the urine gave negative results. The patient was placed on intravenous typhoid vaccine therapy and made slow but steady improvement. On discharge on July 6, there were no sensory disturbances,

and the motor power had improved considerably. When she was seen several months later in the follow-up clinic there were barely any residual motor signs.

Comment.—The febrile onset of the illness and the neural invasion starting with root pain and then motor weakness include this case in our group. We have here again clear evidence of a disease process with the maximum development in the nerve roots. The cases described by Margulies are practically identical with the clinical course in this patient. There were, however, no hyperkinetic manifestations

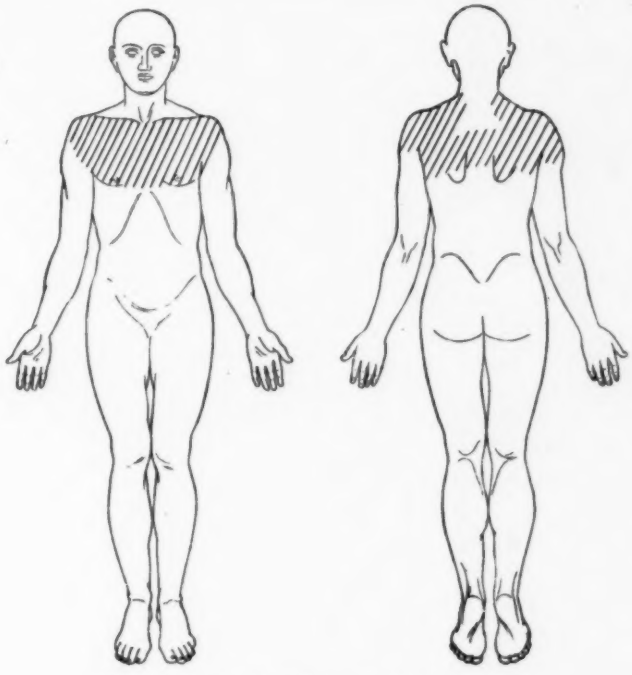

Chart 3 (case 3).—Sensory chart of A. F.

in this case, but it must be borne in mind that she came under observation eight weeks after the acute onset of the illness.

CASE 4.—U. C., a housewife, aged 30, was admitted to the service on March 27, 1926, complaining of numbness in the hands and feet of one week's duration. Six days prior to admission, she noticed a sensation of "pins and needles" in the little fingers of both hands and complained that they felt stiff. The following morning similar paresthesias in the feet were present, and soon after there ensued weakness of the feet, so that she had difficulty in walking. For the two days prior to admission, she could not even stand. Along with the weakness there developed numbness in the hands and feet and tremors on exertion. Cold water in the mouth felt like "pins and needles."

On admission, a flaccid paraplegia with the most marked involvement in the peripheral musculature was present. There was weakness of the back and

abdominal muscles. All the deep reflexes were diminished, and the ankle jerks could not be obtained. A coarse tremor of the extended upper extremities was noted. There was hypalgesia, hypesthesia and thermhypesthesia in the distribution of the third, fourth and fifth lumbar segments and the eighth cervical to the first dorsal segments on both sides (chart 4). The pupils were unequal, the right being larger than the left, and the right pupil reacted sluggishly to light. The speech was nasal, and excursion of the palate was impaired. Examination of the urine gave negative results, and Wassermann tests of the blood and spinal fluid were negative. There were no cells in the spinal fluid. Intravenous typhoid vaccine therapy was instituted, and steady improvement ensued. When the patient was discharged on April 24, there were no positive neurologic observations, except

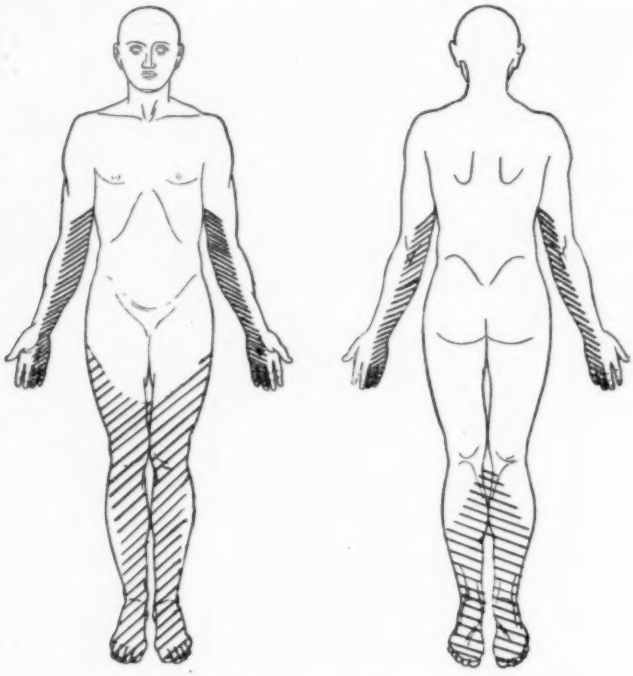

Chart 4 (case 4).—Sensory chart of U. C.

mild tremors of the outstretched fingers. When seen again in the follow-up clinic on July 2, 1926, she had entirely recovered.

Comment.—The involvement of the cranial nerves in this patient, in addition to the radicular syndrome, suggests that the cases described by Bassoe as meningoradicular types of encephalitis might perhaps include this one. The distribution of the sensory changes was radicular and not that usually observed in peripheral neuritis.

Case 5.—L. B., a girl, aged 13, was admitted to the service on Oct. 14, 1926. Six days prior to admission, she had a severe "cold" for three days. She then

noticed that there were weakness and difficulty in climbing stairs, with sharp pain in the back. That night she was awakened by extreme pain in both lower extremities. The following day retention of urine necessitated catheterization, and that afternoon she complained of abdominal and thoracic pain. There then developed numbness and paresthesias in the extremities and incontinence of rectal control. With these complaints she was admitted to the hospital.

On admission, power in both lower extremities and in the muscles of the trunk was diminished. The ankle and knee jerks were obtained; the abdominal reflexes were not elicited; there was a bilateral Babinski sign and hyperalgesia from the twelfth dorsal segment to the toes. Touch was diminished from the twelfth dorsal segment to the toes, as was also vibratory sensation. Position

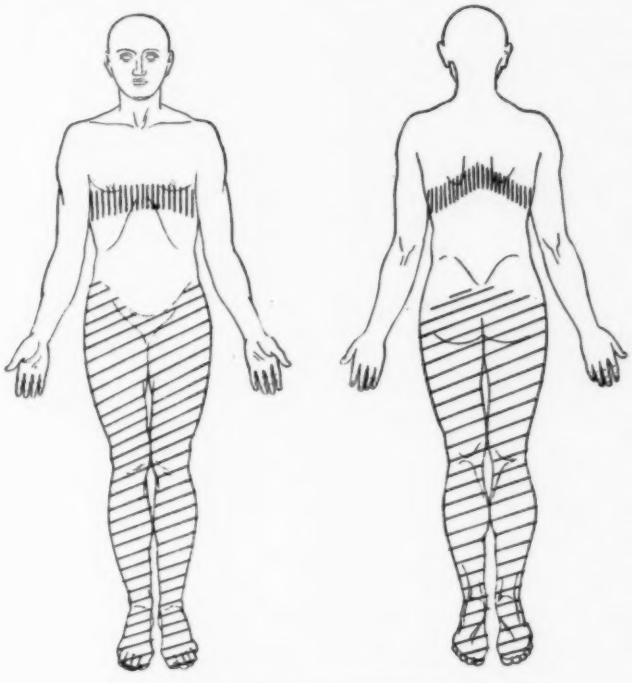

Chart 5 (case 5).—Sensory chart of L. B.

sense was intact, and there was tenderness over the spine from the fourth dorsal to the second lumbar vertebra. The following morning the knee jerks were not obtained, and tactile sense seemed more involved. On October 7, the hyperalgesic zone was limited to the third to the sixth dorsal segments (chart 5). Subjective pain became less intense and on October 19, urinary function had become normal. She continued to improve steadily and when discharged on Nov. 13, 1926, the only vestige of the illness was a slight weakness in the lower extremities and a narrow belt of hyperalgesia of mild intensity in the third to the fourth dorsal segment. In January, 1927, she was seen in the follow-up clinic and was reported as entirely recovered. The complete laboratory study of the case gave negative results.

Comment.—Again there is the typical onset with a respiratory infection followed by invasion of the nerve roots affecting first the posterior and then the anterior roots. The involvement of the cord was more transitory, but while present was definite. The radicular signs were the last objective manifestations to persist. This patient recovered entirely, and when last seen stated that she had no complaints and was attending classes at school.

Case 6.—M. K., a woman, aged 27, was admitted to the service on Dec. 30, 1926. Two weeks prior to admission she had a severe "sore throat and cold"

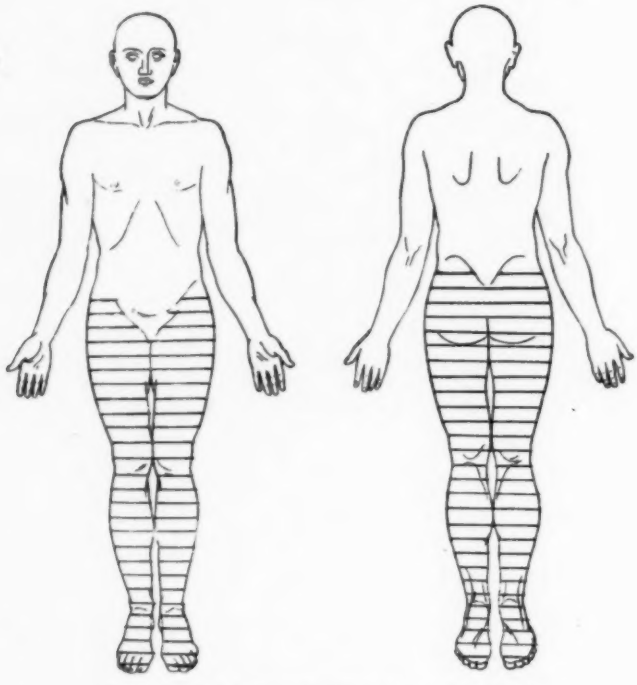

Chart 6 (case 6).—Sensory chart of M. K.

lasting several days. She then noticed that the soles of the feet felt stiff and awkward. She frequently stumbled in walking and could not control the lower extremities. She could not judge the extent of her steps and was not sure of her position on the ground.

On admission, there was no motor weakness in the extremities. All the tendon reflexes were lively. There was a Babinski sign on the right side. No disturbance in touch or pin prick sensation was demonstrated. Muscle sense was markedly impaired in both lower extremities, as was also vibratory sense (chart 6). The urine showed some albumin, but this subsequently disappeared. The Wassermann reactions of the blood and spinal fluid were negative, and there were no cells in the spinal fluid. Throat cultures all gave negative results. She was given a course of intravenous injections of typhoid vaccine. She rapidly

improved and the objective symptoms began to disappear, almost day by day. When discharged from the hospital on Feb. 1, 1927, she was practically well, and when seen subsequently in the follow-up clinic there were no residuals of the illness.

Comment.—Here we have the minimum of root manifestations. The patient was not observed, however, until two weeks after the acute illness. The definite Babinski sign indicates involvement of the pyramidal tract, but otherwise she showed principally a disorder of the sensory pathways.

These six cases have been selected from the group observed in the service, and present in the ensemble the clinical picture that we have designated as myeloradiculitis.

The following case is described, for though due to syphilis, the condition disclosed at operation offers a clue to the probable pathologic process present in our cases.

CASE 7.—F. A., a negro, aged 38, was admitted to the service on Oct. 20, 1925, complaining of inability to walk for four months. He had been married for twelve years. His wife's first two children died in infancy of unknown causes. Two subsequent pregnancies yielded normal children. These two children and his wife were well.

Since 1918, he had been at the Presbyterian Hospital a number of times. The diagnoses were: cholecystitis in 1918, folliculitis in 1920 and syphilis in 1920. The Wassermann reaction of the blood was 4 plus in August, 1918, and after treatment became negative in October of the same year. In May, 1919, it was 2 plus, but on many subsequent examinations was negative. Five months prior to admission, he was examined in the outpatient clinic of the Presbyterian Hospital for complaints of pain and weakness in both lower extremities. The diagnosis at this time was a syphilitic involvement of the spinal cord. Four months before admission, while loading a heavy bale on to a hand truck, he noted a sharp pain in the lower lumbar region of the back. He continued working but shortly thereafter in walking up stairs felt a paroxysm of pain starting in the lumbar region, radiating down the legs and associated with a feeling of weakness. He remained in bed four or five days and received physiotherapy in the form of baking for two weeks at another hospital. The legs continued to grow weaker, until one month before admission when he could no longer walk and the legs felt numb.

On admission, there was a total paraplegia with loss of all forms of sensation below the tenth dorsal segment (chart 7). The knee jerks were diminished, and the ankle jerks could not be obtained. The upper abdominal reflexes were barely elicited, and the lower ones were absent. A bilateral Babinski sign was present. On October 26, a spinal tap revealed no xanthochromia and no block. Wassermann reactions of the blood and spinal fluid were negative, and roentgenograms of the vertebrae gave normal results.

In view of the syphilitic history, the patient received from October 27 to November 19 2.5 Gm. of neoarsphenamine and 4 grains (0.2 Gm.) of mercuric salicylate. The course of the disease remained stationary until at this time another spinal tap showed xanthochromic fluid and a complete block, which at subsequent operation was found to be due to obliteration of the subarachnoid space by the swelling of the spinal cord.

The possibility of a spinal cord neoplasm was then considered, and on November 17, an exploratory laminectomy was performed, the region from the seventh to the ninth dorsal segments being explored. The surgeon described the exposed cord as soft and swollen, suggesting a buttery consistency. There was no obstruction to the probe when it was passed in both directions. Clear, colorless cerebrospinal fluid in large quantity escaped when the dura was opened. When the operating field was closed, the dura was left open.

Seven days later, it was noted that the patient could wiggle the toes of the right foot to a slight degree, and there was a perceptible return of sensation. Steady improvement then continued, and on December 9 there was marked return of motor power, more on the left side, with hypalgesia and thermhypesthesia

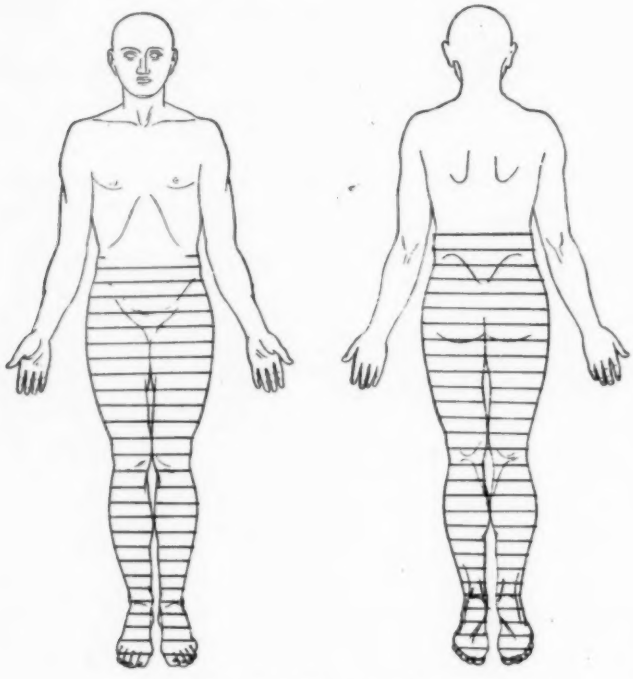

Chart 7 (case 7).—Sensory chart of F. A.

only on the left below the tenth dorsal segment and analgesia on the right below the tenth dorsal segment. Touch at this time was intact, and tuning forks were perceived at both ankles, while position sense had practically returned at the toes. The knee jerks were present; the ankle jerks were not obtained; abdominal and cremasteric reflexes were elicited, but a bilateral Babinski sign still persisted. Improvement continued, and the patient has been seen at the follow-up clinic from time to time. On Oct. 25, 1926, there were no longer any objective complaints. When last seen he had resumed his regular occupation and had recovered entirely.

Comment.—There is some doubt that this patient's syphilis produced the pathologic change in the spinal cord and nerve roots. The

remarkable improvement and recovery, however, are striking, and in this respect the case belongs in the group under discussion. Though syphilitic for many years, the patient finally developed a swollen cord, and only a spinal decompression prevented the persistence of a permanent paraplegia.

It is not our purpose in this communication to discuss neuritic or myelitic syndromes. Mention has been made of these conditions only in their relationship to this group.

In the main all the cases mentioned are characterized by one constant observation—involvement of the nerve roots. Whether the onset is radicular or not, the roots have been found to be uniformly the site of symptoms.

The recovery of all these patients obviously does not permit of any pathologic study. Viewing the group, however, in the light of the condition disclosed by the laminectomy in case 7, one can draw some interesting conclusions. The finding of a swollen cord, which appeared buttery in consistency, and the remarkable recovery after laminectomy reveal the recuperative powers of the spinal cord. And so an inflammatory invasion may produce a similar condition though of milder intensity. Thus, a mild but acute inflammatory disease offers a better prognosis when the cord or roots are invaded than a subacute or chronic infection.

Myelitic syndromes secondary to severe infections are not uncommon. Such patients, when the disease process does not cause a fatal termination of the illness, are bedridden for a lengthy period. Motor and sensory phenomena invariably remain, and the patient becomes a chronic invalid. When a toxic or infectious agent produces a neuritic syndrome there also ensue a long drawn out illness, and frequently permanent physical residual symptoms. In this group, however, we have an unknown infectious agent producing an invasion of the nerve roots and cord of varying severity, ranging from mild radicular symptoms to a fully developed paraplegia. Within an unbelievably short space of time, rapid improvement terminating in complete recovery occurs.

In some of the cases, intravenous injection of typhoid vaccine was used as a therapeutic agent. The remarkable results in the cases, however, are not attributed entirely to this form of therapy. Other patients did just as well without the injections. We feel, however, that the production of an artificial reinforcing resistance in the patient by this form of treatment is worthy of further trial, for in many other instances there has occurred amazing improvement after this form of therapy. Increasing doses of the vaccine are administered intravenously each day. The resulting rise in temperature and the general reaction are an index to the dose required.

SUMMARY

1. A series of cases is presented with acute involvement of the posterior nerve roots and the spinal cord, with rapid recovery from all symptoms.

2. The relation of this myeloradiculitis to infections of the upper respiratory tract is emphasized.

3. Comparison is made with a case of possible syphilitic origin in which laminectomy revealed a swollen cord of buttery consistency, with rapid recovery after spinal decompression.

4. Acute invasion of the nerve roots and cord following mild infections of the upper respiratory tract offers a better prognosis than subacute or chronic infections like syphilis.

5. Mention is made of intravenous typhoid vaccine therapy. This was administered in some of the cases, and while no claims are made that the results were entirely dependent on this treatment, it is felt that further trial of this method of therapy is advisable.

ABSTRACT OF DISCUSSION

DR. FOSTER KENNEDY, New York: The first thing that struck me in these remarkable cases was that they had a definite time incidence. They all seemed to come in the spring of 1926. And that, with a good many of their clinical observations, reminded me of a group of cases that we reported with a somewhat controversial title, "Neuronitis," several years ago, in which an infectious condition implicating principally the nerve roots, occasionally the cranial nerves, was described; in fatal cases changes were found in the spinal cord and as far up as the cortex, with a high incidence of recovery, but with occasionally fatal results.

This group of cases does a good deal to encourage a favorable prognostic state of mind in many infectious diseases of the cord. I have been inclined to be pessimistic in the face of inflammatory diseases implicating the cord and apparently producing a physiologic block, and I have been too quick to say that the physiologic block must necessarily be an anatomic structural block.

Was manometric block manifested in the patients who recovered? The only patient in whom that was noted was the negro who suffered from a syphilitic myelitic condition.

After thinking of these cases, one should be still more chary of the conception of primary degeneration of nerve elements in the cord. We have all, for instance, been brought up to regard a disease such as amyotrophic lateral sclerosis as a primary abiotrophy, a vital lack. I do not believe that amyotrophic lateral sclerosis is a primary degeneration, but I believe that it is the result of a chronic perineural lymphatic toxemia, just as these cases today would seem an acute process of like character.

One sees imitations of amyotrophic lateral sclerosis with segmental root involvement and pyramidal tract involvement produced by syphilis. I have seen it produced by lead, and I am certain that infections in the upper respiratory tract and also toxemias from the intestine are capable of producing degeneration in the spinal cord and roots.

A little while ago, I was able to produce a great improvement in a lumbar cord degeneration by having a prostatic abscess treated, and experience with local contiguous infection in diphtheria throws added light on what can be done in this way.

These are extraordinarily important cases, admirably presented and inspiring in the whole field of infection of the central nervous system.

One might remember, apropos of these cases, that interesting epidemic which occurred in Massachusetts about ten years ago due to streptococcal infection of milk served to hospitals for mental patients, in which many died and many more were affected with generalized polyneuritis, radiculitis and myelitis from the streptococcal toxins propagated to the central nervous system from the intestine.

The more such epidemics are reported, the more knowledge will advance regarding infections of the central nervous system.

Dr. LaSalle Archambault, Albany, N. Y.: The remarkable series of cases presented by Dr. Strauss and Dr. Rabiner, viewed from the standpoint of nosology and pathogenesis, offers a singularly puzzling problem. That such massive disabilities should have been followed by so prompt and integral a recovery is rather startling, and that such extensive involvements of the spinal roots and cord substance should not have been accompanied by consistent changes in the spinal fluid is equally astonishing. However, in some of these cases a lumbar puncture was not performed until two weeks or more after the onset of symptoms, and in one case at least a definite lymphocytosis was present. No mention is made of the presence or absence of tenderness of the peripheral nerve trunks and muscular masses in any of the cases. That the symptomatology observed by the authors indicates predominant involvement of the nerve roots and a varying implication of the cord substance, thus justifying the title "myeloradiculitis," is obvious. It is likewise conceded that a survey of neurologic literature does not reveal any exactly similar group of cases. However, closely analogous syndromes are not wanting, and I am not at all sure that Foster Kennedy's conception of "infective neuronitis" does not apply to the group of cases reported by Dr. Strauss and Dr. Rabiner.

During the World War and within the last decade, a number of cases have been reported from different sources in which the symptomatology, with a few minor exceptions, was essentially the same. The condition was ushered in by variable systemic manifestations, but severe pains in the chest, back and limbs were a striking and constant initial complaint and were followed by rapidly developing flaccid paraplegia or tetraplegia, marked reduction or abolition of the tendon reflexes, impairment of sphincter control, objective disturbances of both superficial and deep sensation and, in a large percentage of cases, cranial nerve palsies affecting more particularly the facial nerve on one or both sides. The spinal fluid was frequently normal, but in some cases a definite excess of globulin was present. The earlier cases of this group were encountered among British and other troops and were variously designated as "acute infectious polyneuritis" by Gordon Holmes, Bradford, Bashford and Wilson, as "infective neuronitis" by Foster Kennedy and as "acute infective meningo-myelo-neuritis" by Casamajor.[9] A fair percentage of these early cases exhibited the clinical physiognomy of Landry's syndrome and went on to a rapidly fatal termination, which perhaps is not surprising in view of the distressing circumstances under which they developed.

Almost at the same time, however, a much more benign type was observed in France and described by Guillain, Barré and Strohl[11] under the heading of "curable acute polyradiculoneuritis." This form was characterized by the same

clinical features minus the bulbar extensions; isolated increase of globulin in the spinal fluid (albuminocytologic dissociation) was a constant observation and complete recovery within a period of a few weeks to a few months was almost the rule. Subsequently, other isolated instances of this curable syndrome were reported in France and elsewhere, the most important of which is that just published by François, Zuccoli and Montus,[13] in which the occurrence of bilateral facial palsy and xanthochromia clearly serves to establish, if not the identity at least the close affiliation between the cases originally observed on both sides of the English Channel. Dr. Rabiner has already pointed out that in this country, in 1920, Bassoe described a group of cases with outstanding meningoradicular manifestations which he regarded as a special clinical type of epidemic encephalitis.

More recently, Bériel and Devic in a series of highly suggestive articles [14] called attention to a number of cases characterized by severe root pains; muscular tenderness; rapidly progressive flaccid motor paralysis frequently predominating in the proximal segments of the limbs; a varying degree of objective sensory loss which, however, never was wanting; abolition of tendon reflexes; decided impairment of sphincter control; occasional implication of the facial and other cranial nerves and, frequently, an excess of globulin in the spinal fluid. Some of these cases proved fatal, but the great majority of patients recovered integrally in from a few weeks to a few months. These authors envisaged their cases as instances of a polyneuritic or myeloradiculoneuritic form of epidemic encephalitis. While this interpretation led to considerable controversy, their views gained considerable favor in many quarters.

In reviewing this hurried and incomplete sketch of the literature one cannot help but feel that all of these cases, catalogued under different designations, have much in common; indeed, the analogies are numerous and striking, the differences negligible. Whether any or all of these various groups actually represent special clinical types of epidemic encephalitis or result from some totally unrelated neurotropic virus cannot of course be answered at this time, but I fail to see wherein the series of cases reported by Dr. Strauss and Dr. Rabiner differs fundamentally from any of them. Barring the exceptionally rapid recovery, the main distinction seems to reside in the escape of the cranial nerves. Even this point is not as significant as it seems, however, as in one case it is clearly stated that "the pupils were unequal, the right being larger than the left; speech had a nasal twang and the palatal excursion was impaired." To my mind it is rather unfortunate that a new name should be coined every time a fresh group of cases arises, merely on the basis of some minor and frequently inconstant differential feature. Even in spite of the absence of anatomic verification, it may logically be argued on purely clinical grounds that most if not all the groups of cases enumerated in the present discussion are simply variants of one and the same underlying pathologic process. The term myeloradiculitis has the advantage of simplicity and adequately expresses the probable pathologic condition in the majority of these cases. Perhaps one should be more cautious regarding the ultimate prognosis in these cases in which prompt recovery occurs, having already learned that an interval of years may elapse between the attack of epidemic encephalitis and the onset of parkinsonism, between the initial retrobulbar optic neuritis and the fully confirmed picture of multiple sclerosis.

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14. Bériel and Devic: Les formes périphériques de l'encéphalite épidémique, Presse méd. **33**:1441, 1925.

DR. ISRAEL STRAUSS: I will first answer the questions that have been put to us.

There was no sign of block, either complete or partial, except in the one case in which there had been a history of syphilis. The man unquestionably was syphilitic. He had received a great deal of antisyphilitic treatment in another hospital. He came to us with a history of syphilis and the symptoms as portrayed on the chart. In view of the fact that syphilis was present we again gave him an intensive course of treatment, without result, and the spinal fluid showed no block at the beginning; subsequently it showed a block and xanthochromia.

There was in this man's history a point not brought out in its recital which may be of importance: When he first complained of pain in the back, he claimed that it came on when he was lifting a heavy case of goods. We were brought face to face with a problem when we obtained the spinal block and decided that a laminectomy was essential, with the result as portrayed.

Whether or not the condition found in this man's cord was syphilitic I am not prepared to say. Even though the Wassermann reaction at that time had become negative in both the blood and the spinal fluid, I cannot state that a syphilitic process could not have been present. However, directly following the laminectomy, the relief of pressure and the improvement were remarkable in their rapidity and completeness.

Therefore, either the trauma in a syphilitic patient may have some relation to the rapid onset of the paraplegia, or there was some factor other than the syphilis involved in the pathologic process.

Dr. Kennedy emphasized the fact that in the presence of cases of this kind, we have to be rather guarded in our prognosis, and it was this rapid recovery that impressed us and gave us the impetus to report this class of cases. Dr. Kennedy also called attention to the fact that all these cases occurred in one year and that there was possibly at this time an epidemic of some mild infectious type. We have subsequently had other cases of this kind. They may, however, be of a sporadic nature.

In answer to Dr. Tilney's questions, I wish to state that our typhoid nonspecific therapy is always administered intravenously. I do not know that the typhoid treatment had any effect in these cases. It is a matter that cannot be decided. We gave it in a few of them. The patients did extremely well. One or two others did not receive treatment. They also did well.

It is only a question of whether or not, in view of the ignorance regarding the effect of nonspecific therapy, one should give a patient the benefit of a possible aid in his recovery.

Herpes was not present in any of these cases, nor was there any history of herpes having been present.

Dr. Archambault says that we have not stated whether or not there was nerve or muscle tenderness. It is a custom in our department sometimes to leave out negative signs and put down only positive signs. There is a danger, of course, in this method, for the reason that one may always question whether the omission of a symptom was intentional or unintentional. In these cases, however, I can state that evidence of peripheral nerve involvement expressed by pain and tenderness along the nerve trunks of the muscles was not present.

As to the question of the uniqueness of this series, Dr. Rabiner and I are fully aware of the cases reported during the war, the literature of which has been extensively gone over by Dr. Archambault; there were also cases described by the English, but as Dr. Archambault said they named these cases polyneuritis—and that is true of much that is in the literature. These are not cases of multiple or polyneuritis. These are cases of involvement of the roots and cord.

There is one case, however, as pointed out by both Dr. Tilney and Dr. Archambault, in which there must have been involvement of the brain stem. There is no reason, however, why occasionally a process of this kind should not involve the upper portion of the neuraxis. But the involvement of the brain stem in this case was slight and, comparable to the other symptoms, of such minimal importance that we did not stress it, although we must admit its pathologic significance.

This brings me to the question of etiology and its relationship to the cases described by Dr. Archambault.

I do not feel that we should call this a new syndrome exactly. I do not feel that we should take it out of that large group of cases already described in the literature under different headings just because it does not compare in every detail with them. The cases reported by Dr. Spiller on the first day of this meeting, under the heading of "Encephalomyelitis Disseminata" may well bear some relation to this type of case. In fact, I regret that our paper was not placed immediately after his, so that the two could have been discussed together. Of course, in our cases autopsy was not performed, and therefore we can not give the definite pathologic condition as Dr. Spiller did in one of his cases, but in considering the question of acute multiple sclerosis and myelitis disseminata, our cases do not come into the discussion. I do not think anyone here would say that these were cases of multiple sclerosis, and I do not believe, either, that one has the right to say that they may develop into it.

In regard to epidemic encephalitis, although I have studied that disease extensively I would hesitate, in the absence of an outspoken epidemic, to make a diagnosis in any case even remotely resembling it as being due to that virus.

PARAPLEGIA IN FLEXION

WITH SUBACUTE, COMBINED DEGENERATION OF THE CORD *

GEORGE W. HALL, M.D.
AND
EDWIN F. HIRSCH, M.D.
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Paraplegia in flexion was described as long ago as 1837, when Ollivier [1] reported Pott's disease with thighs flexed on the pelvis, the legs on the thighs. In 1874, Edes [2] reported this disorder in a patient with a tumor of the cord just below the cervical enlargement. This account has been omitted in other reviews of the literature.

In 1883, Demange [3] reported the disorder in a man, aged 65, who had painful flexion of both legs. Autopsy disclosed two symmetrical regions of softening in the posterior part of three segments of both lenticular nuclei, that on the right extending further into the external capsule and the small mass of gray matter below the anterior extremity of the optic thalamus beneath the middle commissure. No mention is made of disease in the cord.

In 1899 Babinski [4] reported his observations on three patients and the results of postmortem examinations. One of them had a tumor in the right bulbopontile region; another a compression of the cord in the upper thoracic region, and the third, large plaques of sclerosis in different levels of the cord. He emphasized that secondary degeneration of the pyramidal bundles was absent completely in the first and third, and was present in the second case only in traces. In 1911, Babinski [5] reported another account in which he thought the causal lesion was a multiple sclerosis of the cord. In the same article he mentioned compression of the cord, or medulla, by a tumor, and also bilateral lesions of the brain as being possible causes of such a syndrome.

Soques [6] reported a rather typical case following "grip," in which he suspected a sclérose en plaques. Etienne and Gelma [7] reported

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* Read at the Fifty-Fifth Annual Meeting of the American Neurological Association, Atlantic City, N. J., May 29, 1929.

1. Ollivier, C. P.: Traité des maladies de la moelle épinière, Paris, 1837, vol. 1, p. 431.
2. Edes: Boston M. & S. J. **91**:306, 1874.
3. Demange, Emilie: Rev. de méd. **3**:371, 1883.
4. Babinski, J.: Bull. et mém. Soc. méd. d. hôp. de Paris **16**:342, 1899.
5. Babinski, J.: Rev. neurol. **19**:132, 1911.
6. Soques, M. A.: Rev. neurol. **19**:376, 1911.
7. Etienne and Gelma: Rev. neurol. **19**:173 (July) 1911.

another case, in a woman, aged 58, in whom the first symptoms appeared at 20 years of age and in whom an atypical tremor developed resembling that of paralysis agitans. There was no postmortem examination.

Anglada [8] reported the results of an autopsy on a patient with paraplegia in flexion in whom lesions were found in the anterior horns and pyramidal tracts of the cord associated with meningeal and peripheral nerve lesions.

Coyon and Barré [9] reported the case of a patient with von Recklinghausen's disease and a neoplasm of the first motor nerve root on the right side, compressing the cord. Simon, Cornil and Michon [10] observed a similar disorder. The patient of Marie and Foix had symmetrical vascular lesions of the brain. The pyramidal tracts in the upper portions of the cord were intact, but in the lumbar region were changed. There was no primary lesion of the cord to explain the paraplegia.

Bouttier, Alojouanine and Girot [11] reported paraplegia in flexion with parkinsonism and Parinaud's syndrome (vertical ocular paralysis of convergence). The lesion was located somewhere between the locus niger and the pons.

In this country, Schaller and Gilman [12] and A. Gordon [13] have reported histories of patients with the disorder before the American Neurological Association. So far as our investigation of the literature goes, there is only one record of paralysis in flexion with subacute combined degeneration of the cord, and that is reported by H. de Jong.[14]

A woman, aged 69, had paraplegia in flexion with paresthesias in both upper extremities. The reflexes in both the upper and the lower extremities were active, the Babinski sign was positive on both sides, there was marked generalized muscular atrophy and a red and painful tongue. Later, urinary and bowel incontinence appeared, and the achilles reflexes were lost. The erythrocytes were 2,100,000 per cubic millimeter; the color index was 1.38, and the leukocytes were 11,000 per cubic millimeter. There were anisocytosis, poikilocytosis, microcytosis and basophilic granulation of the red blood cells.

A postmortem examination demonstrated verrucous endocarditis of the mitral valves, adenocarcinoma of the lesser curvature of the stomach and arteriosclerosis of the vessels of the brain. In the cerebellum there was a foramen magnum pressure furrow, but there were no other signs of compression. In the second

8. Anglada: Montpellier méd. **33**:73 and 97, 1911; abstr., Rev. neurol. **20**: 261, 1912.

9. Coyon and Barré: Nouv. iconog. de la Salpêtrière **27**:81, 1914.

10. Simon, Cornil and Michon: Soc. de méd. de Nancy, March 16, 1926; abstr., Rev. neurol. **33**:*262*, 1926.

11. Bouttier, Alojouanine and Girot: Rev. neurol. **29**:1514, 1922.

12. Schaller, W. F., and Gilman, P. K.: Spastic Paraplegia in Flexion, Arch. Neurol. & Psychiat. **10**:512 (Nov.) 1923.

13. Gordon, A.: J. Nerv. & Ment. Dis. **62**:354, 1925.

14. de Jong, H.: Acta psychiat. et neurol. **2**:105, 1927.

frontal convolution there were slight vascular changes; the aqueduct of Sylvius was slightly dilated, and there was widening of the third ventricle. In sections of the cord taken from different levels there was degeneration of the lateral and dorsal columns and also of the direct pyramidal tracts. The nerve roots were normal. There was a zone of degeneration in the medulla in the pyramidal tract of the right side only. Muscular atrophy in both lower extremities, with the reaction of degeneration, could not be explained.

REPORT OF A CASE

Clinical History.—A white woman, aged 51, entered St. Luke's Hospital on March 1, 1928, as a patient of Dr. Siegfried Maurer, who has permitted us to study and report her illness. Anemia, cancer, tuberculosis and other serious diseases are not mentioned in the family history. She regarded herself as well until some time in 1925, when occasionally she noticed fatigue and general weakness associated with some abdominal distress. These symptoms grew worse until April, 1927, when she noticed numbness in the large toe on one side. The numbness extended slowly to both feet, and gradually paralysis appeared in both legs so that she walked with difficulty until Aug. 14, 1927, when a lumbar puncture was made. Following this she had a paraplegia in flexion of the lower extremities.

On Aug. 9, 1927, examinations of the blood[15] demonstrated: 65 per cent hemoglobin (Dare); 3,200,000 red cells; 13,600 leukocytes; 58 per cent polymorphonuclear leukocytes; 2 large lymphocytes; 40 per cent small lymphocytes; color index, 1 +; coagulation time, 9 minutes; negative Wassermann reaction of the blood. Stained blood films showed the changes of red cells usual in pernicious anemia. On Aug. 7, 1927, the spinal fluid was clear; the Wassermann reaction was negative; the pressure was 126 mm.; the colloidal gold test gave the result, 0011100000. On Aug. 20, 1927, gastric analysis, with the Ewald test meal, demonstrated: undigested food, absence of free hydrochloric acid and a total acidity of 6 degrees. The urine was negative for albumin, sugar and other abnormal constituents.

Examination and Course.—In April, 1928, the patient had a lemon tint to the skin; the pupils were equal and reacted to light and accommodation. There were no cranial nerve paralyses nor paralyses of the upper extremities. The liver and spleen were not palpable, and the heart and lungs were normal. The abdominal reflexes were not obtained. The lower extremities were in a position of flexion, as shown in figure 1. The patellar and achilles reflexes were lively; Babinski, Chaddock and Gordon signs were positive on both sides. Epicritic sense was diminished over the lower extremities and to a lesser extent over the trunk and upper extremities. There was loss of muscle and joint sense in the lower extremities. Trophic disturbances were absent. The patient experienced difficulty in voiding the urine, and the urinary bladder was distended; the urine was without abnormal constituents. A spinal puncture was made on March 29, 1928. The fluid withdrawn was clear, and there was no "block" in the canal as shown by Queckenstedt's method. The laboratory report of the spinal fluid mentioned no unusual changes. Six days later, the patient complained of severe pains in the legs which gradually grew more severe during the next seven days, when she became delirious and developed slight fever, and incontinence of the bowels and bladder. Cystoscopy demonstrated changes in the bladder such as accompany a lesion of the spinal cord. She died on April 16, 1928.

15. Made by Lattimore Laboratories, Kansas City, Mo.

Postmortem Examination.—No noteworthy changes were demonstrated in the tissues of the trunk except hypostatic hyperemia and slight bronchopneumonia of the lungs. On May 29, 1928, the formaldehyde-hardened brain weighed 1,209 Gm. The cerebral hemispheres were 17.5 by 6.5 cm. wide, and in the temporal region 9.5 cm. high. The convolutions were not flattened, and the sulci were moderately wide; the leptomeninges were thin and faintly opaque. Examination with a hand lens in bright daylight revealed no circumscribed opacities. The olfactory bulbs were symmetrical and unchanged; there were no changes in the optic chiasma, the infundibulum and other external structures of the brain. The leptomeninges between the optic chiasma and the pons were faintly opaque. The basilar and vertebral arteries had thin walls. The cerebellar hemi-

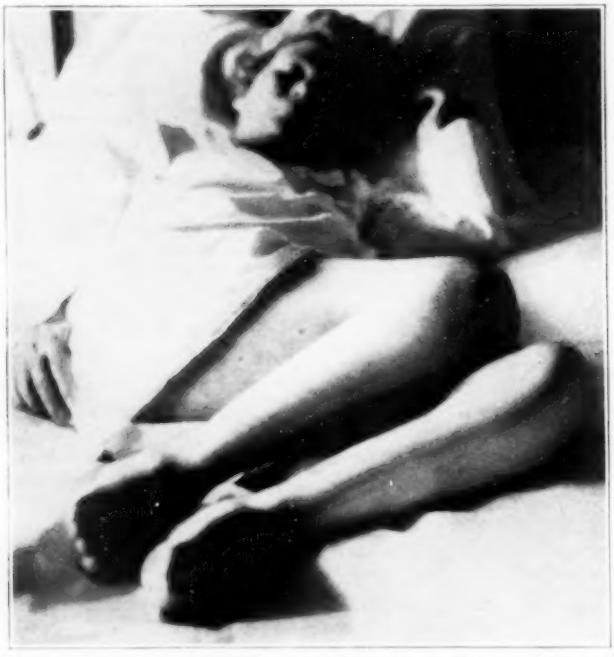

Fig. 1.—Lower extremities of patient in position of flexion.

spheres were symmetrical, and on the tonsilla, corresponding to the impression of the foramen magnum, was a shallow groove. Approximately 7 cm. of the spinal cord was attached. The surfaces made by sectioning the cerebral hemispheres in parallel frontal planes, 1 cm. apart, were unchanged. The lateral ventricles were small, and the ependymal lining was smooth. The aqueduct of Sylvius was 1.5 mm. in diameter. The lining of the fourth ventricle was smooth; the anterior and posterior velums were thin. On surfaces made by cutting the pons and cerebellum at different levels there were no noteworthy changes.

Tissues of the brain from the right and left nucleus lentiformis, the right gyrus occipitalis superior, and the left gyrus occipitalis posterior, the pons, the right and left crus cerebri, the right and left thalamus, including the nucleus ruber and substantia nigra, the right and left cornu ammonis, the right and left gyrus centralis anterior, the right gyrus frontalis inferior, the left gyrus frontalis

Fig. 2.—Photomicrograph showing medial zone of nerve fiber degeneration in the dorsal tracts.

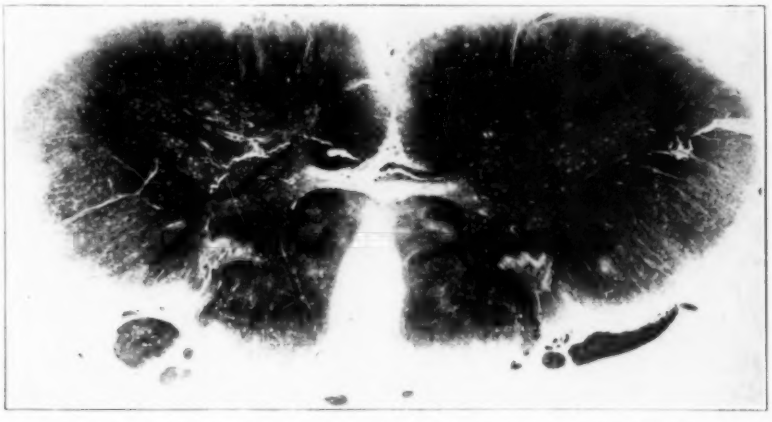

Fig. 3.—Photomicrograph showing slight perivascular round cell infiltration.

medialis, and tissues around the aqueduct of Sylvius were examined microscopically in sections stained with hematoxylin-eosin, and with phosphotungstic acid-hematoxylin. Included in these sections were the leptomeninges from different places, the choroid plexus and the ependyma. In them there were no noteworthy changes of the brain tissues. The cerebral peduncles were stained according to the Pal-Weigert method, and no degeneration of the fibers was found.

The formaldehyde-hardened spinal cord was without macroscopic alterations, except that in the middle and lower thoracic regions the dorsal columns bulged somewhat above the surface of the cord. Tissues for histologic examination were taken at the following levels: olivary body; upper, middle and lower cervical regions; upper, middle and lower thoracic; middle and lower lumbar. These were stained according to the Pal-Weigert and the Bielschowsky methods, with hematoxylin and eosin, and with phosphotungstic acid-hematoxylin. The changes noted at these levels are summarized in the following statements:

Olivary Body: There was a narrow medial zone of nerve fiber degeneration in the dorsal tracts (fig. 2).

Upper and Middle Cervical Region: There was a marked bilateral destruction of the nerve fibers of the fasciculus gracilis, but of no other portions, and along the neural canal was a marked hyperplasia of the ependyma. Around the blood vessels penetrating the involved portions of the cord was a slight perivascular round cell infiltration (fig. 3).

Lower Cervical Region: Extending like a wedge from the dorsal surface of the cord almost to the posterior transverse commissure was a degeneration of the posterior tracts involving the fasciculus gracilis and the fasciculus dorsalis proprius on both sides. There was also a narrow margin of nerve fiber degeneration along both sides of the anterior median fissure involving the fasciculus cerebrospinalis lateralis. There was marked ependymal gliosis along the neural canal. Around the blood vessels of the meninges and the involved tissues of the cord there were round cell infiltrations.

Upper Thoracic Region: The destruction of the posterior columns was much more extensive at this level than in the preceding. It involved, on both sides, the fasciculus gracilis and the medial portion of the fasciculus cuneatus; also included were the medial portions of the fasciculus cerebrospinalis ventralis, the fasciculus cerebellospinalis and the fasciculus cerebrospinalis lateralis. Around the capillaries and small blood vessels of the involved tissues were circular aggregates of large vacuolated (so-called "foam") cells. The ependymal cell hyerplasia and the abundant perivascular round cell infiltrations were noteworthy changes, and the involved portions of the posterior columns bulged beyond the contiguous cord surface.

Middle Thoracic Region: The bilateral destruction of the fiber tracts at this level included the fasciculus gracilis and much of the fasciculus cuneatus. In the lateral columns there was a broad, wedge-shaped destruction of the fasciculus cerebellospinalis and the fasciculus cerebrospinalis lateralis. Of the anterior columns only the medial margin of the fasciculus cerebrospinalis ventralis was included.

Lower Thoracic Region: At this level there was bilateral destruction of the fasciculus gracilis and much of the fasciculus cuneatus in the dorsal columns, also of the fasciculus cerebellospinalis, fasciculus cerebrospinalis lateralis and some of the medial fibers of the fasciculus cerebrospinalis ventralis. The destruction of the nerve tracts was not as extensive in this as in the middle thoracic region. About the neural canal there was hyperplasia of the ependymal cells,

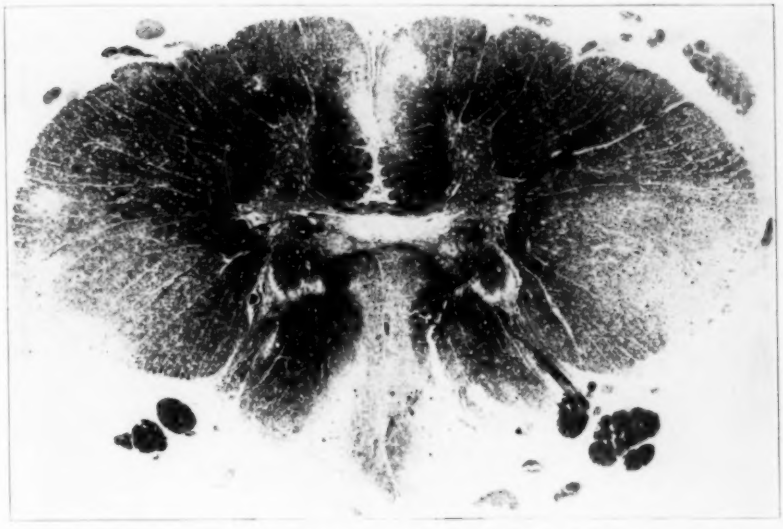

Fig. 4.—Photomicrograph showing marked round cell infiltration and circular aggregates of vacuolated cells.

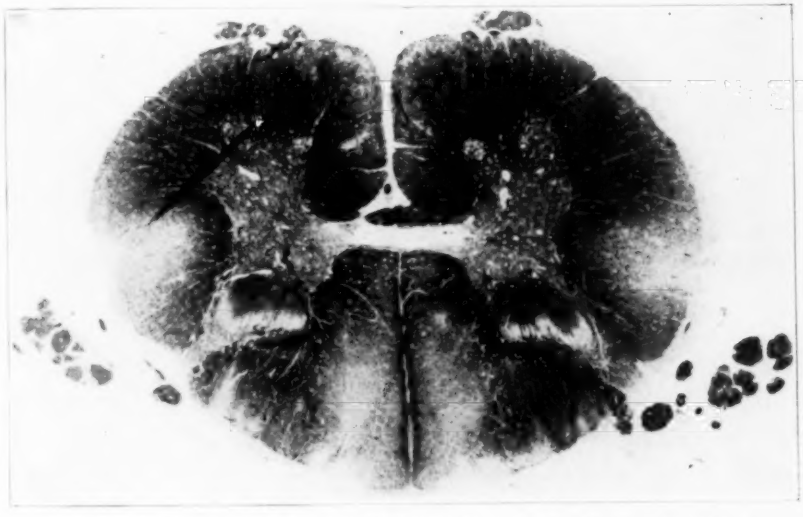

Fig. 5.—Photomicrograph showing intact fibers in the involved regions.

while around the blood vessels, especially in the involved regions, there was a marked round cell infiltration and circular aggregates of vacuolated cells (fig. 4).

Middle Lumbar Region: At this level the tract destruction was limited to the fasciculus gracilis (not the fasciculus cuneatus), the fasciculus cerebellospinalis and the fasciculus cerebrospinalis lateralis. There were no changes in the fasiculus cerebrospinalis anterior. In the involved tracts there were perivascular round cell infiltrations. The degeneration of the tracts was much less extensive, so that in preparations stained according to the Bielschowski method there were many intact fibers in the involved regions (fig. 5).

Lower Lumbar Region: Only a little of the fasciculus gracilis along the posterior median sulcus was destroyed; the changes in the fasciculus cerebellospinalis and fasciculus cerebrospinalis lateralis were much less. The tissue changes otherwise were like those in other levels.

Summary.—The changes in the spinal cord were: extensive fiber degeneration of the posterior and lateral columns and slight fiber degeneration of the anterior columns, especially marked in the mid and upper thoracic regions and diminishing below and above. Around the blood vessels of the involved regions there were marked round cell infiltrations.

ABSTRACT OF DISCUSSION

Dr. W. F. Schaller, San Francisco: In 1923, before this society, and in collaboration with Dr. Phillip Gilman of San Francisco, I reported a case of paraplegia in flexion due to a tumor of the spinal cord on the anterolateral aspect of the cord in the lower cervical region.

The idea that paraplegia in flexion might be due to pressure involvement of the anterolateral aspect of the cord was suggested to me by an article by Babinski, who reported that in cases of paraplegia in flexion observed by him the pyramidal tracts were either spared or very slightly involved; that the Babinski reflex may or may not be present, and that the cutaneous defense reflexes were very much exaggerated.

In this case of Dr. Hall's, it appears that the lesions so typical of combined sclerosis were largely in the posterior and lateral aspects of the cord. I watched particularly for any evidence of patchy degeneration in the anterolateral columns. There was some, but very little, suggestion of it.

This case, therefore, is another well worked up case, for record to solve finally the meaning of paraplegia in flexion.

Dr. Alfred Gordon, Philadelphia: The characteristic symptoms of this syndrome are flexion of the lower extremities by contractures, increase of the defense reflex, absence of exaggeration of knee reflexes or else their total abolition and anatomically an integrity of the pyramidal tract. In the present case the condition of the defense reflex has not been mentioned and at autopsy extensive degeneration of the pyramidal tract was observed. Consequently it differs from the majority of cases reported in the literature from the time of Babinski in 1911. The present case proves, therefore, at first glance, that the symptom group may not always be present in its typical combination. However, there is one feature about the present case which, if closely analyzed, may range it among those of other writers, and this is that the flexor paralysis with contractures made its appearance almost immediately after a spinal puncture. In all the cases that I have observed, spinal or cerebral, the course of events was such that when extensor contractures become replaced by flexor contractures, the prognosis becomes serious and it is indicative of an extension of the original lesion. In this particular respect the

observation of Dr. Hall and Dr. Hirsch is interesting and important. The withdrawal of spinal fluid, otherwise speaking a new physical manipulation of the cerebrospinal axis, aggravated the condition; indeed, their patient became worse rapidly.

From a diagnostic standpoint the state of the defense reflex is important. As is well known, the contraction and the relaxation brought out by stimulation of the skin of the foot are slower in pathologic than in normal conditions, but intensification of this reflex in all the extremities and its extension to other parts of the body are always an indication of grave and diffuse lesions. The reflex is the result of a release in the elementary mechanisms concerned in the activity of the spinal cord which activity becomes exaggerated and misdirected by the underlying pathologic process.

The flexor paralysis under discussion has its physiologic importance, as it points strongly to the possibility of its being the expression of an increased defense reflex thus indicating and suggesting the existence of spinal automatism.

Whether we deal with spinal or cerebral cases, this spinal automatism is due to cerebral interruption by reason of the existing lesion, and in the cerebral cases by release from inhibition or by stimulation of the cord below the cerebral lesion.

Commencing with Sherrington, many experimental investigators in the field of decerebration have proved that the same physiologic mechanism underlies the flexion, extension, crossed extension and "mark time" reflexes; namely, that they all represent phenomena of spinal automatism similar to those which are observed in the decapitated frog. Whether the interruption of the cerebro-medullo-spinal continuity occurs in the spinal cord or high up in the cerebrum above the mesencephalon, whether the interruption is bilateral or unilateral, the deduction that can be drawn from all these cases is that the spinal automatism is created by pathologic interruptions which physiologically speaking mean suppression of cerebral inhibition.

In flexor paralysis (cerebral or spinal) the automatism of the lower centers is intensified not only in purely reflex movements but also in volitional acts, so that in all such cases stimulation from without as well as an attempt on the part of the patient to perform an act with his affected limb will increase the flexion contracture. At any period of a given disease the latter is an indication of a more serious organic lesion. In my cerebral cases it is precisely the state of this hypertonicity without distinct pyramidal signs that I had good reason to attribute to the function of the extrapyramidal system.

The analysis of the course of the paralysis, the observation of the state of the defense reflex and the transformation in some cases of extensor contracture into flexor contracture are all indications of the extension of the pathologic process.

In spite of some differences in the main symptomatology, the case presented is a valuable addition to our collection of analogous cases and presents a new element, namely, the occurrence of flexor paralysis in a combined degenerative state of motor and sensory tracts in the spinal cord.

BILATERAL ACOUSTIC NEUROFIBROMAS

A CLINICAL STUDY AND FIELD SURVEY OF A FAMILY OF FIVE GENERATIONS WITH BILATERAL DEAFNESS IN THIRTY-EIGHT MEMBERS *

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In the Neurosurgical Clinic of the University of Pennsylvania Hospital there are records of sixty-two verified cases of tumor of the cerebellopontile angle. Two of these are cases of bilateral acoustic neurofibromas, one of which was associated with generalized neurofibromatosis while the other was not. This survey was suggested by a statement in the history in the latter case which intimated deafness and blindness in a number of the family connections for five generations. It so happened that eleven of the twelve members of the second generation of this family migrated to another state, so that this survey covered chiefly the direct descendants of only one of the original twelve progenitors. In this family there were thirty-eight cases of bilateral deafness; fifteen of these persons subsequently became blind. In each case in which a history was obtainable it was found that headache and vomiting preceded the blindness. From the evidence obtained from living relatives, the prevailing lesion was bilateral acoustic neurofibromas.

Generalized neurofibromatosis has long been known as a familial disease. In 1882, von Recklinghausen [1] stated that "multiple neuromas cannot be considered as a purely acquired disease. . . . The congenital disposition in these cases is unmistakable, but we have still to explain why the skin tumors appear in some cases and not in others. This may be due entirely to a difference in postnatal factors." In 1922, Hoekstra [2] collected a large series of cases of this disease illustrating

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1. Von Recklinghausen: Ueber die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuromen, Berlin, A. Hirschwald, 1882.

2. Hoekstra, Geert: Ueber die familiäre Neurofibromatosis mit Untersuchungen über die Häufigkeit von Heredität und Malignität bei der Recklinghausenschen Krankheit, Virchows Arch. f. path. Anat. **237**:79, 1922.

a hereditary tendency. The present report, however, deals with a family that exhibits a particular expression of the disease, namely, bilateral acoustic neurofibromas. In this family other manifestations of the disease are almost entirely lacking. Also, the condition in this series of cases seems to follow the mendelian principles with a remarkable degree of exactness.

Probably the first recorded examples of bilateral tumors in association with central neurofibromatosis are those of Wishart,[3] in 1822, and Knoblauch,[4] in 1843. In 1910, Henschen [5] assembled a series of 136 cases of unilateral acoustic tumors and 19 cases of bilateral tumors. In 1915,[6] he added to this 109 cases of unilateral tumors and 5 cases of bilateral tumors. This made a total of 245 cases of unilateral acoustic tumors and 24 cases of the bilateral lesions. Of the 24 cases of bilateral tumors, 19 were associated with other evidences of von Recklinghausen's disease, while of the cases of unilateral tumors only 5 were so associated. Since 1915, there have been reported 18 verified cases of bilateral acoustic tumors associated with neurofibromatosis [7] and two verified cases of isolated bilateral tumors. This makes a total of 37 cases

3. Wishart, J.: Cases of Tumors in the Skull, Dura Mater and Brain, Edinburgh M. & S. J. **18**:393, 1822.

4. Knoblauch: De neuromate et gangliis accessoriis, Inaug. Diss., Frankfort, 1843.

5. Henschen, F.: Ueber Geschwülste der hinteren Schädelgrube, insbesondere des Kleinhirnbrückenwinkels, Jena, Gustav Fischer, 1910.

6. Henschen, F.: Zur Histologie und Pathogenese der Kleinhirnbrückenwinkeltumoren, Arch. f. Psychiat. **56**:21, 1915.

7. Bassoe, P., and Nuzum, J.: Report of a Case of Central and Peripheral Neurofibromatosis, J. Nerv. & Ment. Dis. **42**:785, 1915. Christin, E., and Naville, F.: À propos de neurofibromatoses centrales, leurs formes, etc., Ann. de méd. **8**:30, 1920. Symonds, C. P.: Case of Bilateral Eighth Nerve Tumors Associated with Multiple Neurofibromata and Multiple Endothelioma of Meninges, J. Neurol. & Psychopath. **2**:142, 1921. Shea, J. J.: Acoustic Neuromas, Laryngoscope **32**:460, 1922. Bielschowsky and Henneberg, R.: Histologie und Histogenese der zentralen Neurofibromatose, Libro en honor de S. R. y Cajal, Madrid, 1922. Steurer, Otto: Ueber Beteiligung des inneren Ohres und des Hörnerven bei multiples Neurofibromatosis Recklinghausen, mit besonderer Berücksichtigung der sekundär absteigenden Degeneration des Hörnerven, Ztschr. f. Hals-, Nasen- u. Ohrenh. **4**:124, 1922, 1923. Herrman, G., and Terplan, K.: Ein Beitrag zur Klinik und Anatomie der Kleinhirnbrückenwinkeltumoren, Ztschr. f. Neurol. u. Psychiat. **93**:528, 1924. Jacobson, V. C.: Fibroma of Acoustic Nerve, Am. J. Path. **1**:259, 1925. Schmincke, A.: Zur formalen Genese des Teratoma diphyllicum, Ziegl. Beiträge z. allg. path. u. pathol. Anat. **73**:502, 1925. Höglund, G.: Multiple Neurofibromatosis, Acta psychiat. et neurol. **1**:145, 1926. Ayala, G., and Sabatucci, F.: Clinical and Pathologic-Anatomical Contribution to Study

associated with neurofibromatosis and 7 cases [8] which were apparently unassociated with other evidences of the disease.[9] Thus, as has been mentioned (Cushing [10]), when bilateral acoustic tumors are proved to exist, they are usually found to be merely an expression of the more widely disseminated disease.

The foregoing figures would seem to indicate that unilateral and bilateral acoustic tumors are two separate and distinct disease entities. This view is corroborated on a pathologic basis by Penfield.[11] The isolated unilateral tumors to which he has applied the term "perineurial fibroblastomata" contain nerve fibers only in the capsule. In the tumors of von Recklinghausen's disease, however, the nerve fibers will be found to penetrate the tumors with but few exceptions. Therefore, the tumors of this latter disease constitute the true neurofibromas.

The frequency with which von Recklinghausen's disease appears in bilateral, symmetrically distributed nodules has been called to our atten-

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of Central Neurofibromatosis, Ztschr. f. d. ges. Neurol. u. Psychiat. **103**:496, 1926. Steurer, O.: Zur Klinik und Pathologie der Neurofibromatosis des Gehirns und des Hörnerven, zugleich ein beitrag zur Klinik des psychogenen Hörstörungen, Folio Oto-Laryngol. **14**:154, 1925-1926. Ostertag, B.: Geschwülstbildungen im Schädeldach bei allgemiener Recklinghausenscher Krankheit, Verhandl. d. deutsch. path. Gesellsch. **21**:293, 1926. Firket, J.: Maladie de Recklinghausen centrale, tumeurs pontocérébelleuses bilatérales et méningiomes multiples, Ann. d'anat. path. **3**:407, 1926. Heine, L.: Zwei Doppelfälle von Tumor des Kleinhirnbrückenwinkels mit und ohne Neurofibromatose, Ztschr. f. d. ges. Neurol. u. Psychiat. **100**:481, 1925 (cases 1 and 2). Frets, G. P.: Central Neurofibromatosis: A Case, Nederl. Tijdschr. v. Geneesk. **1**:930, 1928.

8. Sutton: The Lateral Recess of the Fourth Ventricle, etc., Brain **9**:352, 1886 (cases 1 and 4). Stewart and Holmes: Symptomatology of Brain Tumors, Winther, 1904. Henschen, F.: Ueber Geschwülste der hinteren Schädelgrube insbesondere des Kleinhirnbrückenwinkels, Klinische und anatomische Studien, Jena, Gustav Fischer, 1910, p. 12. Leroux, L.: Total Deafness from Bilateral Tumor of the Cerebellopontine Angle, Rev. de laryng. **44**:453, 1923. Günther, H., and Manasse, P.: A Study of Acusticus Tumors, Ztschr. f. Hals-, Nasen- u. Ohrenh. **9**:516, 1924. Strauss, Israel; and Globus, J. H.: Intracranial Tumors: Clinical and Anatomical Observations on a Group of 12 Cases of Brain Neoplasm, S. Clin. North America **8**:321, 1928.

9. In one of these cases reported by Leroux (footnote 8, fourth reference) it is stated that a brother died with similar symptoms. No necropsy was obtained, however. In addition, another case is reported by Biggs (Case of Multiple Intracranial Tumors with Involvement of Both Auditory Nerves, Lancet **2**:14, 1909) in which bilateral recess tumors were associated with a solitary tumor of the falx cerebri.

10. Cushing, Harvey: Tumors of the Nervus Acusticus, Philadelphia, W. B. Saunders Company, 1917.

11. Penfield, W.: The Encapsulated Tumors of the Nervous System, Surg. Gynec. Obst. **45**:178, 1927.

tion by Preisser and Davenport.[12] These authors also described several families in which the principal tumors are similarly located in certain parts of the body in succeeding generations. This family resemblance in the distribution of the tumors and also the bilaterality are strikingly shown in the series of cases herein reported. An interesting point which has not as yet been definitely settled is this: Do the perineurial fibroblastoma and the neurofibroma have the same seat of origin on the acoustic nerve? Several very early cases of acoustic tumors are described in the literature, but in most of them it is not perfectly appar-

Fig. 1.—Reproduction of Henschen's illustration showing a small tumor lying within the right porus acusticus internus. *A* indicates the auditory nerve, *V* the vestibular nerve, *F* the facial nerve and *B* the blood vessels.

ent with which type of lesion the authors are dealing. In all of them, however, the small nodules were found on the peripheral portion of the nerve at the internal auditory meatus. Usually the vestibular portion of the nerve was more involved than was the auditory. In 1915, Henschen made a reconstruction in wax of an early acoustic tumor which was discovered by chance at necropsy. In this reconstruction (fig. 1), it is evident that the vestibular portion of the nerve is primarily

12. Preisser, S., and Davenport, C. B.: Multiple Neurofibromatosis and Its Inheritance, Am. J. M. Sc. **156**:507, 1918.

involved. The facial and auditory nerves seem to be separate and distinct from the tumor mass. The vestibularis, however, spreads out over the proximal end of the tumor and gradually disappears into the substance of the tumor, to reappear at its distal end.

The predisposition of the eighth nerve to the development of tumors may perhaps be explained on an embryologic basis, as has been suggested in a recent report by Skinner.[13] Skinner stated his belief that the type cell of these tumors in the neurilemma sheath cell,[14] and he illustrated the reasons for the presence of this particular cell in unusual numbers in the peripheral portion of the vestibular nerve. He agreed with Henschen that the tumor originates in the peripheral part of the vestibular division of the eighth nerve. He concluded with the statement that the vestibular reactions in suspicious cases are of primary interest and may yield valuable information on the subject of early diagnosis. The cases about to be reported yield clinical corroboration to Henschen's statement that the tumor originates on the vestibular division. Early cases are described in which the vestibular responses are lost while hearing remains little, if at all, affected.

This investigation, begun in January, 1929, was stimulated by a most unusual family history of hereditary deafness, furnished by a patient whose record follows.

REPORT OF CASE

Clinical History.—VA 6 (fig. 9), a man, aged 28, was admitted to the neurosurgical service of the University Hospital on Oct. 9, 1928, having been referred to the clinic by Dr. T. K. Wood, of Muncy, Pa., who apparently was the first physician to recognize the unique hereditary tendency of the disease in this family. The chief complaint was deafness and blindness. The history of the patient's illness was essentially a repetition of a common complaint which had affected many members of his family for five generations. The patient complained of partial deafness which began at the age of 17. Whether he became gradually deaf in both ears coincidentally, or whether there was a difference in the onset of loss of acuity of hearing in the right and left ears is not known. The deafness, however, progressed steadily and became complete six weeks prior to admission, coincidentally with a beginning failure of vision. Failure of vision progressed rapidly, and total blindness had been present for two weeks prior to admission. Since the onset of complete deafness there had been considerable vomiting. Vertigo and a staggering gait had been present for four months. Whether or not tinnitus was a symptom could not be determined.

Examination.—Physical examination revealed the following positive observations: The patient was well developed and showed some evidence of loss of weight. He was totally blind and deaf, but was able to talk. He was quite

13. Skinner, H. Allan: Origin of Acoustic Nerve Tumors, Brit. J. Surg. **15**:440, 1929.

14. On this point, however, he differed from Penfield, who stated that the tumors are primarily fibroblastic.

drowsy, but when awakened was fairly alert. He was well oriented and cooperative. In order to communicate with him, it was necessary to spell out the words on the patient's right palm, using his left index finger to draw the letters. He made few mistakes.[15]

On neurologic examination, it was found that the patient's gait was slow and unsteady. He staggered to the right and left, and after walking a short distance he usually fell backward. He fell backward in the Romberg test. There was dysmetria in the finger-to-nose test on both sides. The heel-to-knee test was well performed. In testing for dysdiadokokinesis, the movements were slow but well coordinated. There was no spontaneous nystagmus. The pupils were 4 mm. in diameter and fixed to light. Ocular rotations were limited in all direc-

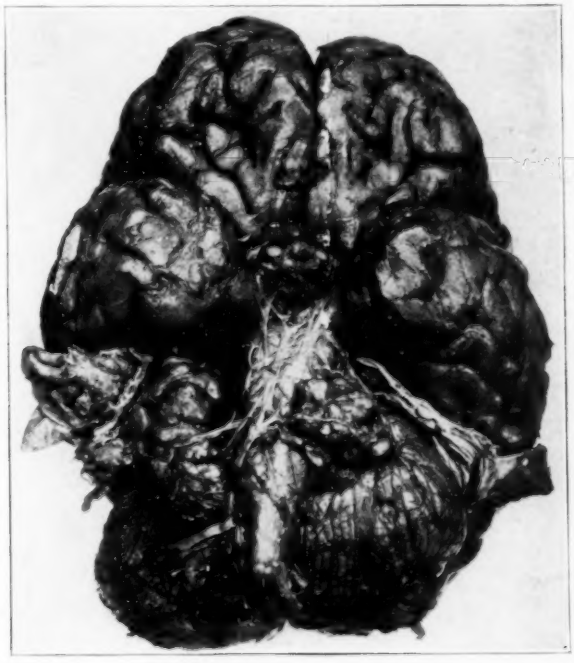

Fig. 2.—Patient VA 6. The larger tumor on the right is attached to the dura.

tions, but particularly in external rotation of the left eye. There was bilateral loss of sense of smell and total blindness in both eyes. Examination of the fundi revealed a choking of 9 diopters in the left eye and of 8 diopters in the right with numerous hemorrhages. The corneal reflexes were slightly sluggish. There was no evidence of involvement of the seventh nerve. There was total deafness in both ears. The ninth, tenth, eleventh and twelfth nerves revealed

15. It is a curious fact that all of the members of this family who became deaf and blind used this method of receiving communications from the outside world; that is, provided that their education was sufficient to enable them to read and write prior to the onset of blindness. This method of communication has been given the name of "graphaesthesia" by Spiller in his lectures to the students at the University of Pennsylvania.

no abnormality in function. The speech was slow, but the words were spoken clearly. All the tendon reflexes were equally diminished. There were no pathologic reflexes. An audiogram disclosed a loss of hearing of 100 per cent in each ear. The Wassermann reactions of the blood and spinal fluid were negative. Roentgenograms of the skull revealed no abnormalities except a suggestion of erosion of the inner portion of each petrous ridge. Bárány examination by Dr. Lewis Fisher revealed that the eighth nerves were entirely nonfunctioning in both the cochlear and the vestibular portions.

Course.—A diagnosis of bilateral acoustic tumors was made. A suboccipital craniectomy was performed on Oct. 30, 1928, by Dr. Frazier. A large right acoustic tumor was found and partially removed by the intracapsular method.

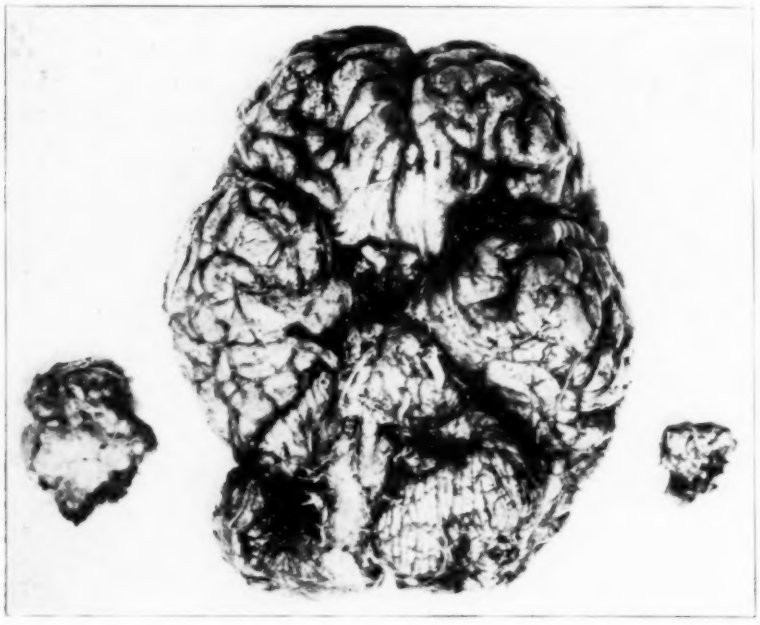

Fig. 3.—Patient VA 6. The superior surfaces of the tumors and their beds after removal.

No tumor was seen in the left recess, but a careful search was not made. The postoperative course was stormy, and the patient died three days after operation with a hemorrhage of undetermined origin into the ventricles.

Postmortem Examination.—A necropsy was performed by the pathologic department under the direction of Dr. E. B. Krumbhaar. The spinal cord was not removed. Except for the condition of the brain, nothing of importance was disclosed.

After removing the calvarium, the operative site was explored before removing the brain. On the right side a tumor mass could be palpated beneath the dura. The nodular mass of the tumor was in close relation to the petrous portion of the temporal bone. At the internal auditory meatus there was a distinct excava-

tion of the bone, apparently caused by pressure of the tumor. On the left side a smaller tumor was found lying on the acoustic nerve just as it entered the bone and, by chipping away the bone on this side, a smaller tumor mass was found lying within the bone.

The brain was unusually large for an adult male brain (fig. 2). The dura showed no abnormality. The veins were markedly injected, giving the specimen

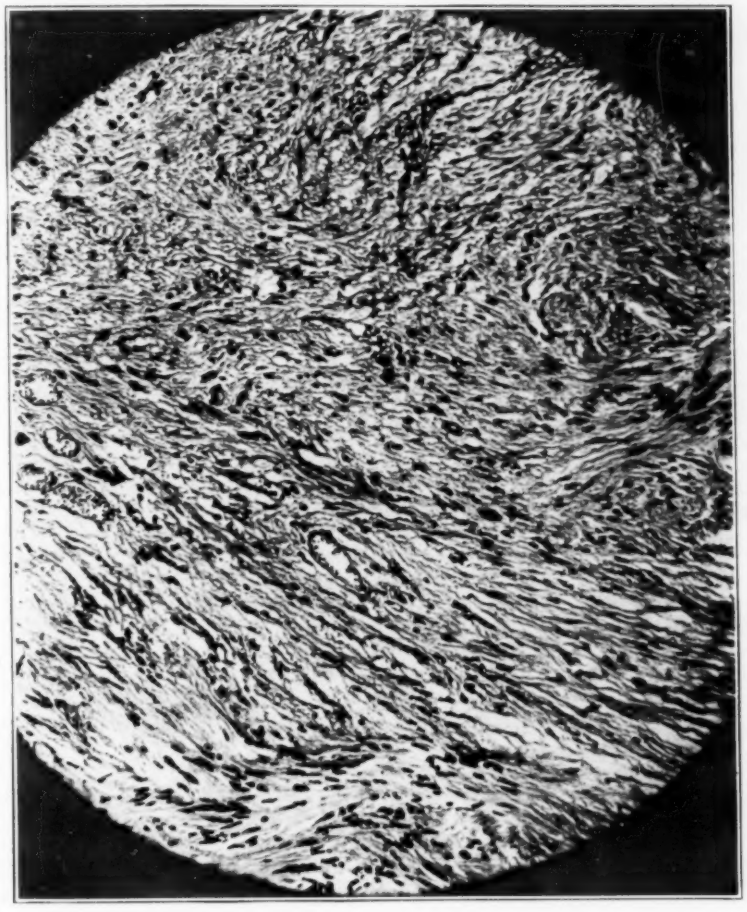

Fig. 4.—Patient VA 6. Fibrous streams with interspersed areas of looser reticular nature. A suggestion of palisading is evident to the right of the center. Hematoxylin and eosin stain; × 160.

a rather cyanotic appearance. The tumor on the right side was rather firmly attached to the dura. It caused a marked compression of the right cerebellar hemisphere. A portion of it had been removed and there was some softening of the inferior surface of the right cerebellar lobe apparently due to operative trauma. The pons was compressed on both sides by the pressure of the tumors,

but much more so on the right than on the left. The tumor on the right measured 5.5 by 3.5 by 3.5 cm. The tumor on the left measured 3 by 3 by 1.5 cm. The gross appearance of the tumors was identical except for the difference in size. They were firm, encapsulated and lobulated. The cut surface had a granular appearance.

As the remnant of the tumor on the right side was dissected from its bed, the proximal portion of the right eighth nerve was found, measuring 4 mm. in

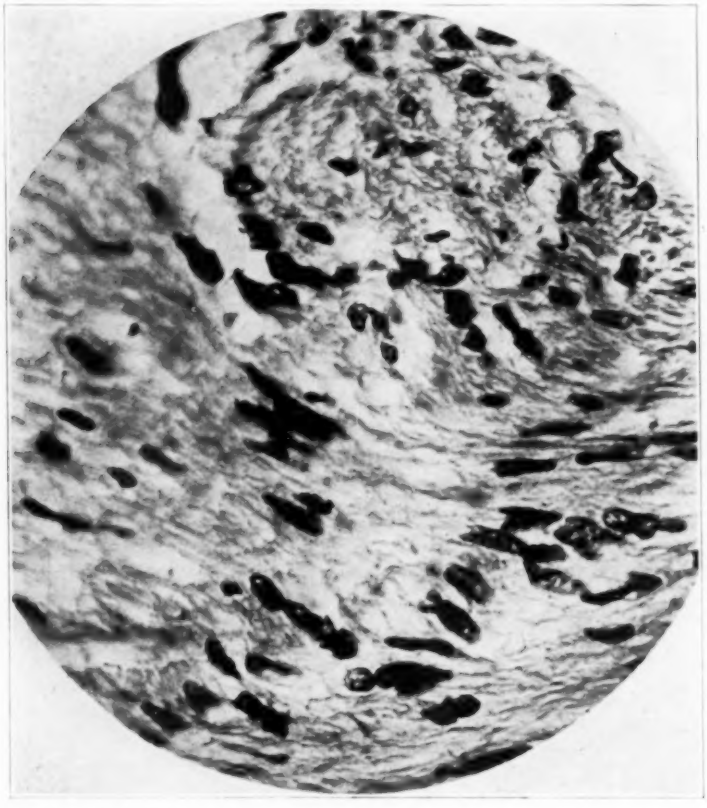

Fig. 5.—The same field that is shown in figure 4, but under a higher power; × 627.

length before it plunged into the substance of the tumor on its mesial aspect (fig. 3). At its point of exit from the tumor mass, it was in close relation to a small nubbin of the tumor which may or may not have been situated in the internal auditory meatus. The seventh nerve was ribbon-thin and almost transparent, and stretched out over the mesial aspect of the tumor to join the eighth nerve at its point of exit. The right fifth nerve was greatly elongated, measuring 3.75 cm. Practically all the cranial nerves on this side of the brain had been stretched by the growth of the tumor. On the left side, the eighth nerve was seen to plunge into the tumor tissue at a distance of 1.5 cm. from its point of

exit from the brain stem. It was entirely incorporated in the mesial aspect of the tumor for the comparatively short distance of 1 cm. before it made its exit. The left seventh nerve was extremely flattened and wound about the superior mesial aspect of the tumor to join the eighth nerve at its point of exit from the tumor. The fifth nerve on this side was also slightly elongated. The remaining cranial nerves showed comparatively little displacement. There were no demonstrable tumors on the dura. There were no tumors on the other cerebral nerves.

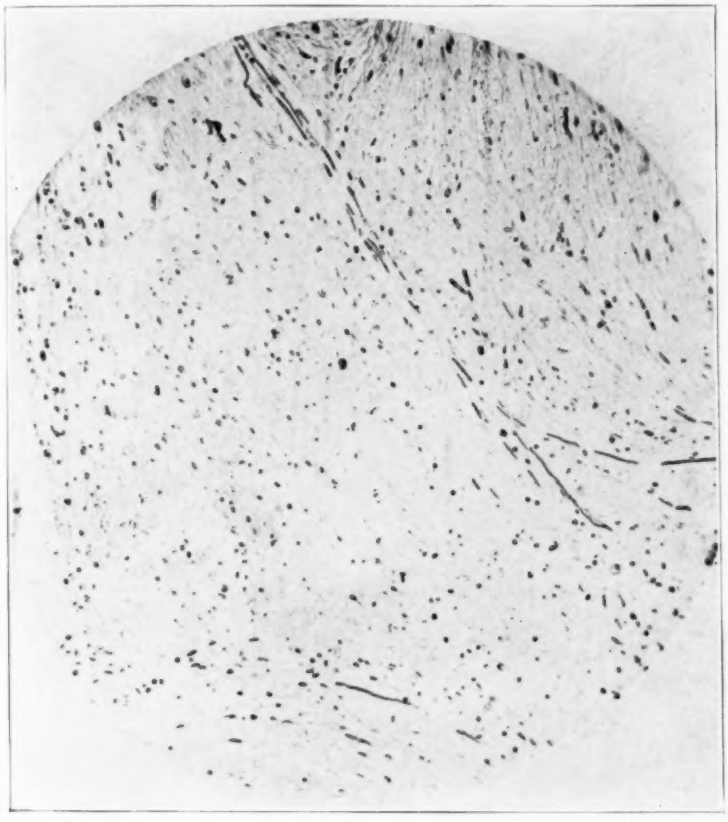

Fig. 6.—Patient VA 6. Nerve fibers are seen invading the tumor tissue. Gross-Bielschowsky stain; × 160.

A horizontal section through the entire brain revealed a slight dilatation of the ventricular system with hemorrhage throughout, which appeared to be recent.

The gross diagnosis was: (1) bilateral acoustic neurofibromas, (2) slight ventricular dilatation with intraventricular hemorrhage and (3) marked injection of the cerebral vessels.

Histologic examination of the tumor tissue by the hematoxylin-eosin stain disclosed interlacing streams of connective tissue fibers with interspersed areas of a looser reticular nature (tissue types *B* and *A* of Antoni[16]). In some of the

16. Antoni, N. R. E.: Ueber Rückenmarkstumoren und Neurofibrome, Stockholm, München and Wiesbaden, 1920.

fibrous streams there was a faint suggestion of nuclear palisading (figs. 4 and 5). On staining by the Gross-Bielschowsky method it was evident that nerve fibers actually penetrated the tumor tissue and not the capsule alone (figs. 6 and 7). Therefore, the lesions were not of the nature of the ordinary isolated perineurial fibroblastomas in which the nerve fibers are present only in the capsules.

The histologic diagnosis was: acoustic neurofibromas (von Recklinghausen's disease).

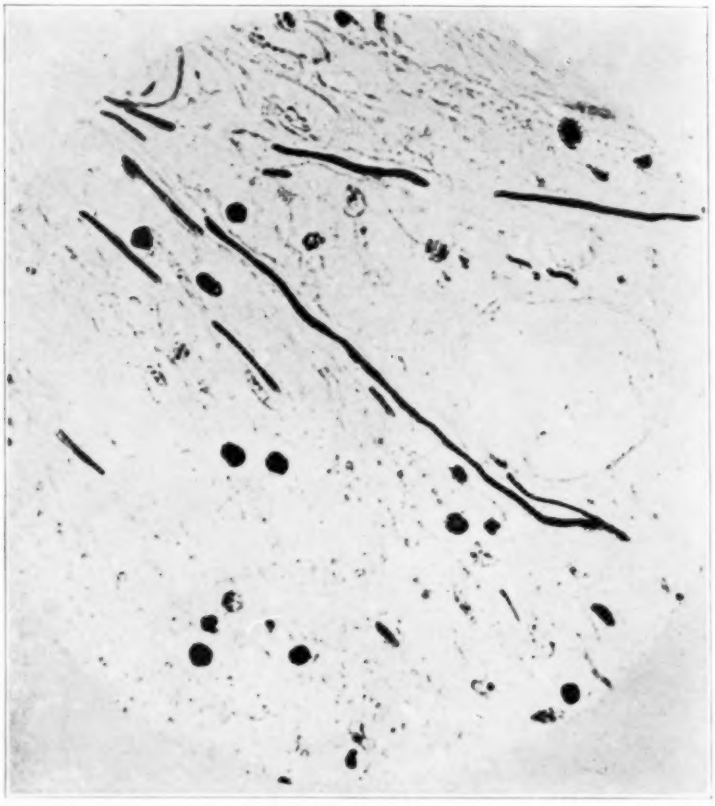

Fig. 7.—The same field that appears in figure 6, but under a higher power; × 627.

THE FAMILY TREE

A complete family tree of the patient extending over five generations was finally compiled. It included 217 members (figs. 8 and 9). Although there were many members of the sixth generation living, none of these were included on the charts as they were as a rule too young to cooperate in the examination. Forty-seven members of this family were interviewed and personally examined. In many instances the information was not as complete as it should be. Any one who has attempted field work of this nature can appreciate the reasons for this. Most of the members were residents of the state of Pennsylvania, and the

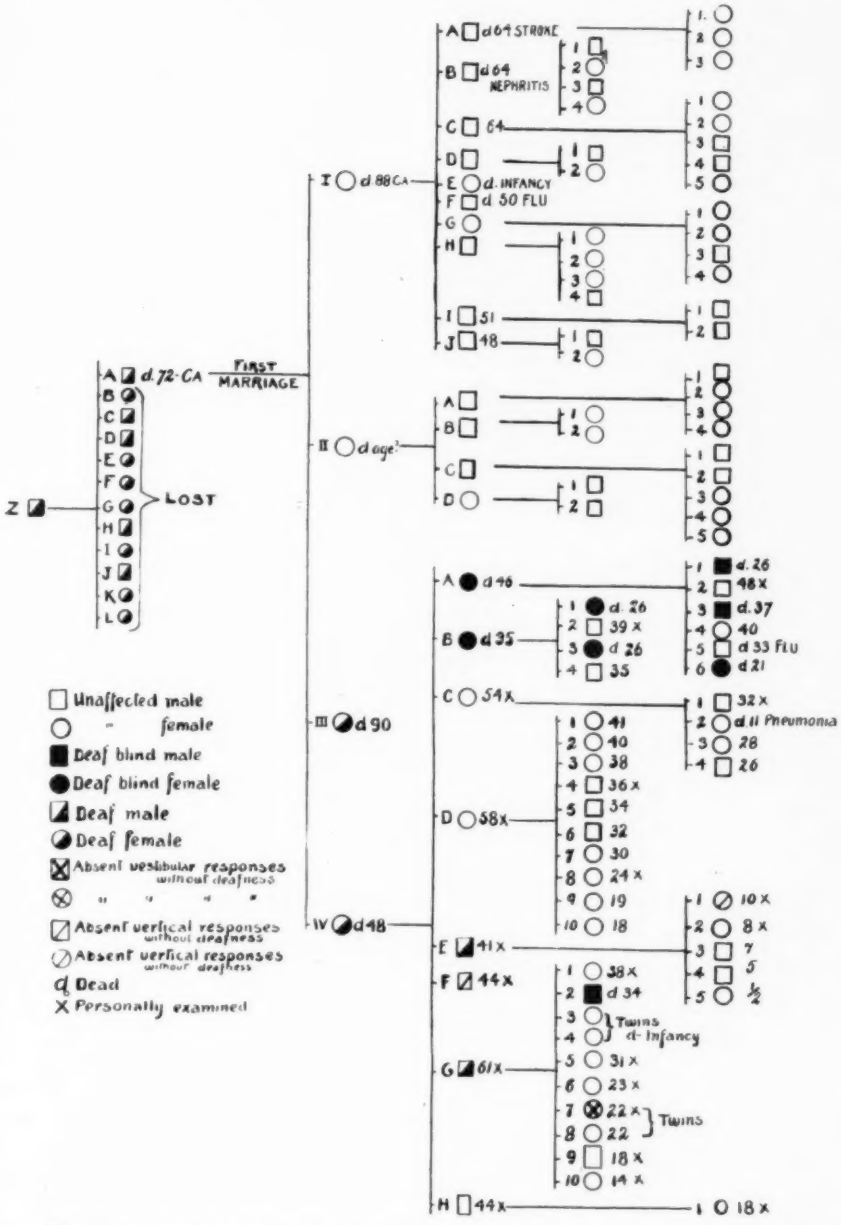

Fig. 8.—The first generation is represented by *Z*, the second by *A* to *L*, the third by roman numerals, the fourth by capital letters and the fifth by figures. The fifth generation consists of a double column. The ages, when known, are placed after the symbols. For the sake of simplicity, the issue of the two marriages of *Z A* are separated. The cause of death, when known, is indicated.

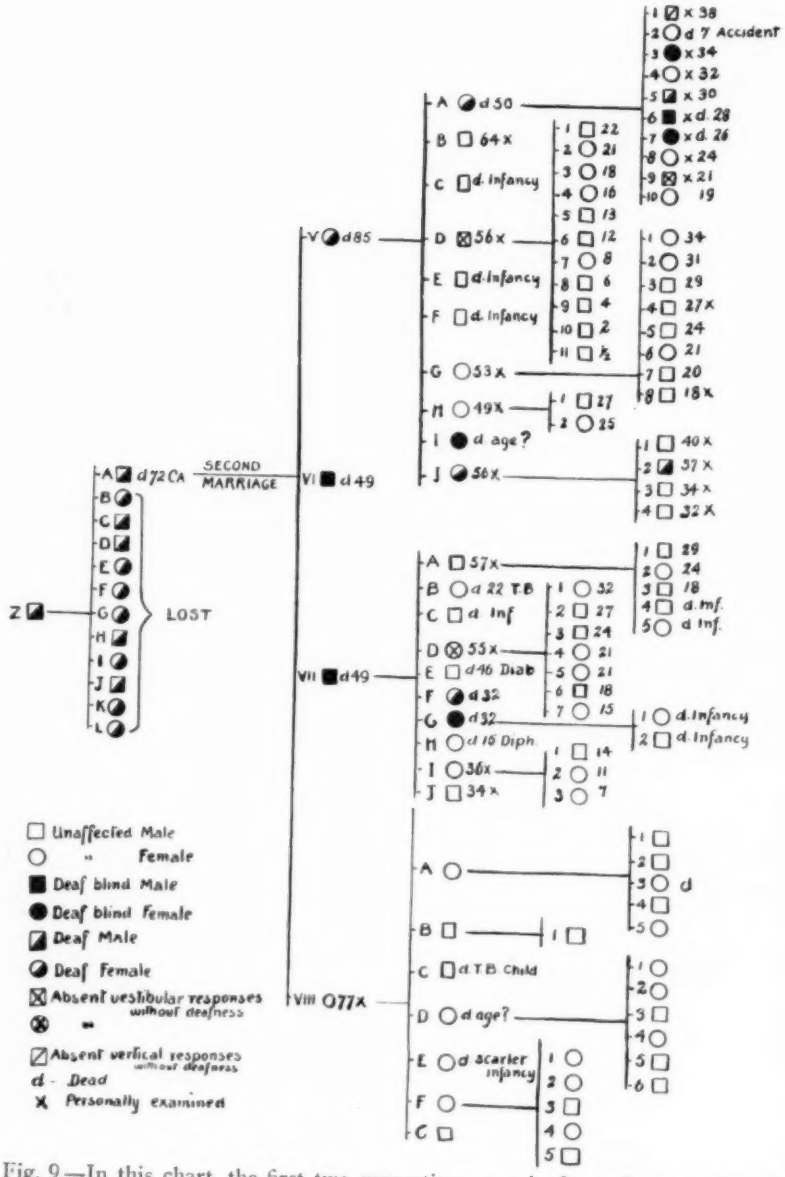

Fig. 9.—In this chart, the first two generations seen in figure 7 are duplicated.

majority lived within a radius of 50 or 75 miles of one another. Even so, they were rather difficult of access. The country was hilly and the roads were not of the best. The persons were found to live in outlying districts, and the addresses obtained were inadequate. The main obstacle, however, lay in the attitude of the subjects. They were almost universally poor. Many of them were ignorant and unable to read or write. Few possessed a telephone. An attitude of unwillingness, fear or suspicion was frequently encountered. Flat refusals of cooperation were occasionally received from the unaffected members. A careful examination of the body surface for the skin manifestations of generalized neurofibromatosis was not requested in these persons for fear of arousing their antagonism.

In the routine examination each subject was questioned carefully as to tinnitus, impairment of hearing, vertigo, otorrhea, headache, vomiting, staggering, difficulty in walking after dark, nodules or pigmented areas in the skin, pain or numbness of the face, spasm or paralysis of the face and impairment of vision. In the examination of the cranial nerves, only tests of smell and taste were omitted. An otoscopic examination was made in each instance. The hearing was tested by means of three tuning forks of 64, 256 and 2,000 double vibrations. In a few of the earlier examinations, forks of 50, 200 and 2,000 double vibrations were used. The Weber and bone conduction tests were performed with the middle fork. The cerebellar examination consisted of an examination for spontaneous nystagmus, past pointing and dysmetria. The normal station and gait were observed as well as the reactions to the heel-to-knee and Romberg tests. The pelvic girdle movements were tested. The vestibular reactions were examined either by turning in the Bárány chair or by cold douching or by both methods. In some cases, the subjects would permit the turning tests but not the douching; in other cases, it was vice versa. Roentgenograms of the skull were obtained in most of the affected members and in several of the unaffected ones. Wassermann examinations of the blood were made when they seemed indicated, provided the subjects were willing. Most of the roentgenologic examinations were performed at the Geisinger Memorial Hospital in Danville, Pa., by Dr. Sidney Hawley through the courtesy of Dr. H. L. Foss. A few of the roentgenologic examinations were performed at the University Hospital in the department of Dr. H. K. Pancoast.

For the sake of simplicity, the matings were omitted from the charts. In only one instance was there an intermarriage, and that occurred between unaffected members of the fifth generation. The information obtainable concerning the first two generations was rather scanty and was furnished by the only living member of the third generation (VIII, fig. 9). This member, a woman, aged 77, had an unusually retentive memory, which was encouraged, no doubt, by her inability to read or write. She never attended school on account of the deafness of her father, Z A, which necessitated her being constantly with him to act as interpreter. This woman (VIII) did not recall her paternal grandfather or uncles and aunts, as they moved west prior to her birth, but she recalled from information furnished by her father that they all subsequently became deaf.[17] She was certain that her father and paternal grandfather were "stone deaf." Regarding the location or offspring of her paternal uncles and aunts, there was no information. Her father, Z A, married twice, there being four children born to each wife. Two of the children of the first marriage subsequently became

17. This point, of course, requires further corroboration, but for the present it is recorded on the charts as an established fact.

totally deaf, as did likewise three of the second marriage. Two of the deaf children of the second marriage died at the age of 49 with headache, vomiting and subsequent blindness. The father, Z A, who was deaf for many years, died at the age of 72 with cancer of the face.

The first member of the third generation (I) was not deaf, and died at the age of 88, with cancer of undetermined origin (fig. 10). This woman was the mother of ten children and the grandmother of twenty-six, none of whom became deaf, although one grandchild (I H 3) was born deaf. This child was examined. Although both auditory nerves were practically nonfunctioning, the vestibular portions were preserved. Therefore, the diagnosis of acoustic tumors could be excluded in this case. No other members of this branch were examined, but it was determined from several sources that there were no other cases of deafness.

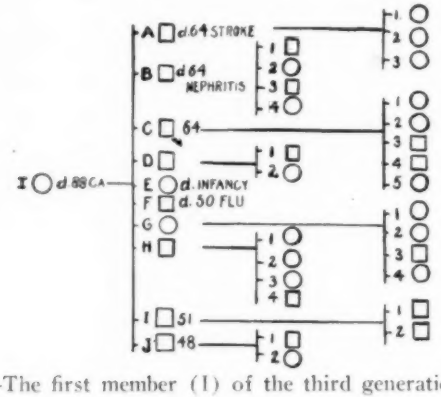

Fig. 10.—The first member (I) of the third generation and descendants. All were unaffected.

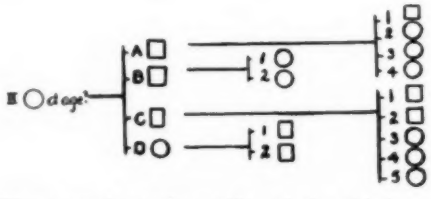

Fig. 11.—The second member (II) of the third generation and descendants. All were unaffected.

II, also unaffected, was the mother of four children and the grandmother of thirteen (fig. 11). None of these descendants subsequently became deaf, according to report.

III became deaf. The age of onset was not known. She married but bore no children, and died at the age of 90 (fig. 12).

IV became deaf, but died of other causes at the age of 48. The age of onset of deafness is not known. She was the mother of eight children, four of whom subsequently became bilaterally deaf.

IV A died deaf and blind at the age of 46. She was said to have been totally deaf for "five or six years at least," and blind for one year prior to death. She was the mother of six children, three of whom became deaf and blind:

IV A 1, a boy, became totally deaf at the age of 23. He became blind at the age of 24 and died at 26.

IV A 2, aged 48, had complained of occasional bilateral tinnitus for seven or eight years. There was no impairment of hearing. His other cranial nerves were normal, and his reactions to turning in the Bárány chair were normal. He was the father of six children. As these children represented the sixth generation, they were not included on the chart. His two eldest children, aged 21 and 19, respectively, gave normal Bárány reactions.

IV A 3 became deaf, but the age of onset was not known. He became blind at the age of 32, and died at the age of 37. He had no children.

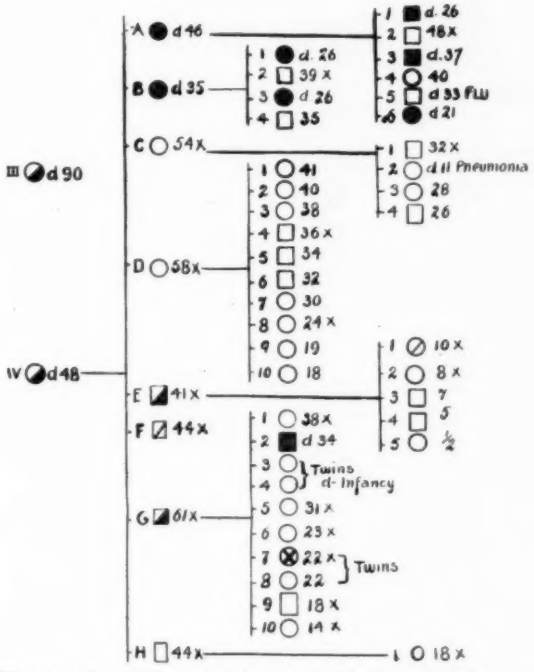

Fig. 12.—The third member (III) of the third generation, and the fourth member (IV) and descendants.

IV A 4, according to reports at the time of this study, was living and well at the age of 40 and was the mother of five children, none of whom were said to be deaf. This member was not examined.

IV A 5 was not deaf, but died of influenza at the age of 33 years.

IV A 6, the youngest member of this family, became deaf at the age of 16 and blind at the age of 20 and died at the age of 21. She was the mother of one daughter who was not examined.

Reverting to the fourth generation, IV B (fig. 12) was a daughter who died at the age of 35. She was said to have been deaf for many years and was blind for one year prior to death. She was married and had four children, two of whom were affected:

IV B 1 was deaf for six years and blind for one year, and died at the age of 26. She had no children.

IV B 2 was living at the age of 39. He had no children. The observations of this subject were interesting. He stated that he could usually tell when his relatives were beginning to be affected, by their staggering gait, as that usually preceded deafness. Examination of his cranial nerves gave normal results, and douching of the right ear yielded normal vestibular responses. Therefore, the diagnosis of acoustic tumors was considered as excluded in his case.

IV B 3 died at the age of 26. She was deaf for two or three years and blind for one year. She was the mother of one child, a girl, aged 15, who was not examined, being of the sixth generation.

IV B 4, aged 35, was living, but was not available for examination.

IV C, aged 54 (fig. 12), was free from symptoms suggestive of acoustic tumor. Her cranial nerves were normal and the vestibular responses on douching the right ear were normal. She was the mother of four children, three of whom were living and not deaf:

IV C 1, aged 32, complained of no symptoms suggestive of acoustic tumor with the exception of an occasional attack of vertigo. His cranial nerves were normal. The vestibular responses on turning and douching ruled out the possibility of such a disease. He was married, however, to a second cousin (V A 8) who was the unaffected daughter of an affected parent. They had no children. IV C 2 died of pneumonia at the age of 11 years. The remaining two children (IV C 3 and IV C 4) in this family were not examined.

Reverting again to the fourth generation, IV D (fig. 12) was living at the age of 58. Her history was unimportant. However, she was one of the few members of this family in whom subcutaneous nodules were present. She had a soft swelling on the anterior aspect of the right wrist and another in the right axilla, each measuring about 1 by 2 inches, resembling lipomas. They were not tender or painful and had been present for about twenty years.[18] The examination of this subject's cranial nerves revealed no abnormality. The vestibular responses on turning and douching were found to be normal. She was the mother of ten children ranging in age from 18 to 41, two of whom were examined:

IV D 4, aged 36, complained of no symptoms suggestive of acoustic tumor. He denied the presence of any skin manifestations and his vestibular responses ruled out the possibility of such a lesion.

IV D 8, aged 24, had been deaf since childhood. She complained of frequent tinnitus which was not lateralized. She exhibited no nodules on the visible portion of the skin. Examination of the cranial nerves gave negative results except for rather sluggish corneal reflexes and a marked impairment of hearing. She could not hear the tone of the 64 fork or of the 2,000 fork in either ear. She heard the 256 fork at a distance of ½ inch (12.7 mm.) in each ear, and air conduction was greater than bone conduction. Examination of the ears revealed a slightly thickened drum on the right side and a normal drum on the left. There was no history of aural discharge. This subject's vestibular reactions, though sluggish, were sufficiently active to rule out the possibility of acoustic tumor. The other brothers and sisters of this family were not examined.

IV E, aged 41 (fig. 12), stated that he had been completely deaf in the right ear since the age of 18, with increasing deafness in the left ear for six years.

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18. Each member of this family who was interviewed was questioned closely about the presence of any nodules or pigmented areas on the body and they all denied such a condition. A careful search for the nodules was not possible, however, because of their unwillingness to cooperate, and considerable tact was necessary in order to make possible even a meager examination.

He was now able to hear only a very loud voice. He did not complain of either dizziness or vertigo. There had been no aural discharge. He gave no history of tinnitus in the right ear, although he had had occasional tinnitus in the left ear for twelve years. His hearing was always worse when he had a cold. His voice had been husky for the past six years. He had no difficulty in swallowing. He was the father of five children, none of whom was deaf. Their ages ranged from 6 months to 10 years. On examination, this patient was found to exhibit no cerebellar signs. The Romberg sign was negative. There was no dysmetria, past pointing or nystagmus. The only nodule on the visible portion of his body was a small wen on the scalp. Examination of the cranial nerves gave negative results except for the following: There was a dense cataract in the left eye. There was no choking of the right optic disk. The corneal reflexes were bilaterally sluggish. Hearing was apparently entirely absent in the right ear, and the subject perceived the vibrations of only the 256 fork at a distance of 1 inch (2.5 cm.) in the left ear. Air conduction was greater than bone conduction. There was no lateralization in the Weber test. The ear drums appeared normal. The vestibular responses on both turning and douching were entirely absent. A roentgenogram of the skull revealed no abnormality. The view of the petrous bones, however, was not entirely satisfactory from the technical standpoint.[19] This subject, therefore, presented the picture of bilateral acoustic tumors. Examination of his children yielded the following data:

IV E 1, aged 10, complained of no symptoms suggestive of an acoustic tumor except bilateral tinnitus which had been present for more than a year. She stated that she had a discharge from one ear several years previously. Examination of the drums revealed no abnormality. The hearing was found to be normal, with a slight lateralization to the right in the Weber test. Examination of the extremities revealed what appeared to be a congenital dislocation of the right hip. There were no positive cerebellar signs. On turning in the Bárány chair, the subject gave reactions that were somewhat subnormal for the horizontal canals. The nystagmus persisted for thirteen seconds on turning to the right and for fifteen seconds on turning to the left. On cold douching of the ears, it was not possible to obtain a response from either vertical canal, although both horizontal canals were found to be functioning. Whether or not this indicated an extremely early stage in the development of acoustic tumors is problematic. IV E 2 had no suggestive history. The ear drums appeared slightly roughened. There were no positive cerebellar signs. There was no lateralization in the Weber test, and the reactions on turning were practicaly normal. On account of the age of the patient, douching was not possible. The remaining three children (IV E 3, IV E 4 and IV E 5) were too young to cooperate, and therefore were not examined.

IV F, a man, aged 44 (fig. 12), complained of no symptoms suggestive of acoustic tumor and denied the presence of any skin manifestations. Examination of the cranial nerves revealed no abnormality. Examination of the ears revealed

19. This particular view of the petrous bones was taken with a Buckey diaphragm inclined at an angle of 22 degrees. With the patient in the supine position and the head flexed, the film was placed under the occiput. The central ray was directed downward and forward so as to pass through the anterior hair line and the foramen magnum. In this position, the posterior surfaces of the petrous bones should appear in profile on the film. This method was described by Pancoast (Significance of Petrous Ridge Deformation in Roentgen-Ray Diagnosis and Localization of Brain Tumors, Am. J. Roentgenol. **20**:201, 1928).

a normal drum on the right side with impacted cerumen on the left. He would not permit the removal of the latter. The hearing was normal on the right and subnormal on the left. On douching, no response could be elicited from either vertical canal, and the responses of both horizontal canals were exceedingly sluggish. Whether these observations indicated also an exceedingly early stage in the development of an acoustic tumor is questionable. This subject was the father of five children ranging in age from 1 to 11 years. Unfortunately, these children were omitted from the chart. None of them was examined. However, the eldest child appeared to have a congenital dislocation of the right hip. This condition was present also in a cousin (IV E 1).

IV G (fig. 12), a man, aged 61, gave the following history: He had been totally deaf for over twenty years. He thought that the deafness began in the left ear, although he was not certain. Bilateral tinnitus probably began after deafness. It sounded like "a bumblebee in a bottle." He complained of occasional attacks of headache associated with vertigo. He denied the presence of any lump in the skin, and none appeared on the visible portion of his body. The cranial nerves were found to be normal with the exception of the fifth and the eighth. There was a moderate hypalgesia in the distribution of the left fifth nerve, and the left corneal reflex was slightly sluggish. Examination of the ear drums disclosed no abnormality. Hearing was apparently entirely absent in both ears. The subject was unable to read or write, and received communications by reading the lips. There was no choking of the optic disks. There were no positive cerebellar signs. The Romberg sign was negative. There was no spontaneous nystagmus. There was no past pointing or dysmetria. Roentgenograms of the skull revealed no abnormality. There was no evidence of erosion of the petrous portions of the temporal bones, although the films were not entirely satisfactory. The vestibular responses were entirely absent on both turning and douching. This subject, therefore, in all probability had bilateral acoustic tumors. He was the father of ten children:

IV G 1, aged 38, complained of no symptoms suggestive of acoustic tumor. There were no positive cerebellar signs. The examination of the cranial nerves yielded negative results. The Bárány reactions on turning were normal. This subject seemed to have escaped any taint.

IV G 2, a man, died deaf and blind at the age of 34, in 1926. He was examined at the United States Naval Hospital, League Island, Pa., in 1924. A report on this patient was furnished us through the courtesy of Dr. E. O. Crossman of the United States Veterans Bureau. At the age of 26, the patient began to suffer from tinnitus of the left ear. Six months later, tinnitus began in the right ear. The hearing subsequently gradually became defective, being worse in the left ear. At the age of 31, the patient was completely deaf in the left ear and could hear the spoken word in the right ear but could not interpret it. He complained of dizziness, weakness and was almost unable to walk after dark. The latter condition had existed since shortly after the onset of tinnitus. He had had some diplopia. He was found to have an ataxic gait. There was a horizontal nystagmus on lateral rotations. The conjunctivae were slightly injected. The Romberg sign was markedly positive. There was incoordination in the finger-to-nose test with intention tremor. The speech was somewhat scanning and staccato. Roentgenograms of the head revealed an erosion of the posterior clinoid processes. The Wassermann reaction of the blood and cerebrospinal fluid and the colloidal gold reaction were negative. Examination revealed complete deafness in each ear to tuning fork tests. The ear drums appeared to be normal. Examination of the fundus disclosed swelling of the optic disks with contraction

of the arteries. This man died two years and eight months after his discharge from the Naval Hospital. He is said to have become almost entirely blind. Necropsy was not performed, but with this history there is small room to question the fact that this patient had bilateral acoustic tumors.

IV G 3 and IV G 4 were twins who died in infancy. IV G 5, a woman, aged 31, had an unimportant history. Examination of her cranial nerves gave negative results. There were no positive cerebellar signs, and the Bárány reactions on turning were normal. She was the mother of six children ranging in age from 3 to 18 years. These children, who represent the sixth generation, were not examined. IV G 6, aged 23, was likewise examined and found to be normal.

IV G 7, aged 22, was one of twins. Four years previously, she fainted for no apparent reason. After this it was noticed that there was a slight drawing of the face to the left. She had been unsteady on her feet for at least five years and was scarcely able to walk after dark. She denied the presence of any skin manifestations of von Recklinghausen's disease. The examination of her cranial nerves revealed nothing abnormal except a questionable hypalgesia in the distribution of the left fifth nerve. The left corneal reflex was sluggish. The ear drums appeared normal. There was no spontaneous nystagmus and no spontaneous past pointing. She swayed slightly in the Romberg position. She was totally unable to walk in the heel-to-toe test, although ordinarily her gait was fairly steady. When the horizontal canals were tested by turning, no response was elicited. There was no response when the right ear was douched for one minute and thirty seconds, at which time the test had to be discontinued on account of the nervousness and apprehension of the patient. We consider the diagnosis of early acoustic tumors in this case as probable. It is unfortunate that the opportunity was not afforded for examining this patient's twin sister (IV G 8). From descriptions furnished by relatives, however, it seemed probable that they were not identical twins. If they were not identical twins, the twin sister need not have carried the defect.

IV G 9 and IV G 10, aged 18 and 14 years, respectively, were examined and found to have normal vestibular responses in the turning test and no history or observations suggestive of acoustic tumor.

IV H, a man, aged 44 (fig. 12), with an unimportant history, denied the presence of skin nodules, with the exception of a small, firm, movable nodule on the forehead. This was neither painful nor tender, and had been present for a long time. Examination of the cranial nerves gave negative results. Hearing was normal, and there were no positive cerebellar signs. The reactions of the horizontal canals on turning were slightly subnormal, but the examination could not be completed because of the reluctance of the patient. On account of the presence of chronic ulcers of the right leg, a Wassermann examination of the blood was made and was found to give a positive reaction. This subject was the father of one child:

IV H 1, aged 18 years, complained of no symptoms suggestive of acoustic tumor, and her vestibular reactions on turning were sufficiently active to exclude the presence of such a lesion.

To revert once more to the third generation, V was a woman who died at the age of 85 (fig. 13). She was deaf for many years, but the exact age of onset was not known. She was the mother of ten children, three of whom died in infancy. Of the remaining seven, three became deaf.

VA, who died at the age of 50, was completely deaf for many years prior to death. She was said to have died of a stroke. She was the mother of ten children, four of whom became deaf:

V A 1, a man, aged 38, complained of no suggestive symptoms except occasional tinnitus after being in a noisy atmosphere. He denied the presence of any skin manifestations and none was evident on the visible portions of this body. The cranial nerves were normal with the exception of bilaterally sluggish corneal reflexes. There were no positive cerebellar signs. On douching the ears, there was no response elicited from either vertical canal. There was a response, however, from both horizontal canals although it was exceedingly sluggish. It consisted of a horizontal nystagmus of poor amplitude, and there was no past pointing after douching. Examination of the ear drums disclosed no abnormality. This subject was considered as possibly having the condition in a latent stage of development.

V A 2 died at the age of 7 as the result of an accident.

V A 3, aged 34, was totally deaf and blind. She was referred to the neurosurgical service of the University Hospital in 1923, by Dr. T. K. Wood of Muncy,

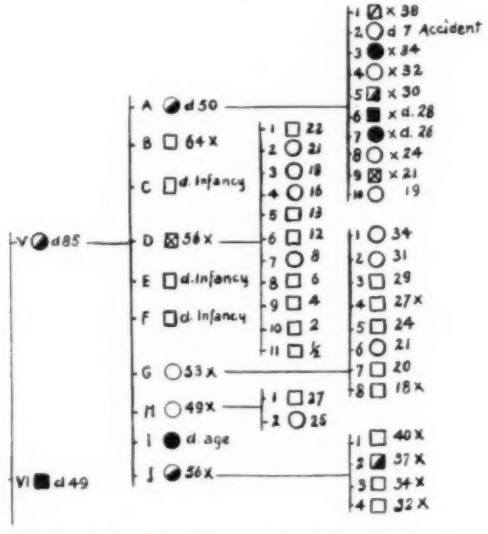

Fig. 13.—The fifth member (V) of the third generation and descendants; the sixth member (VI).

Pa., and Dr. A. F. Hardt of Williamsport. She was admitted on August 8 with a chief complaint of deafness, blindness and headaches. Except for complete deafness, which had been present for the previous seven years, the patient was well until February, 1923. At this time she gave birth to a child and shortly afterward began to have headaches and dimness of vision. She became totally blind a month later. A few weeks later, persistent vomiting appeared, projectile and not related to the taking of food. The vomiting ceased, although the headaches continued until admission to the hospital. On examination, this patient was found to be totally blind and deaf. She had a marked right-sided facial paralysis of the peripheral type. The tongue was protruded to the right. The gait was unsteady and uncertain. The Romberg sign was positive. The patellar and achilles reflexes were bilaterally diminished. There was no Babinski sign. Roentgenograms of the skull revealed beginning convolutional atrophy. The pressure of the cerebrospinal fluid was 32 mm. of mercury. The Wassermann

and colloidal gold reactions were negative. The Bárány report by Dr. Lewis Fisher was: "Repeated douchings reveal no responses except possibly from the left horizontal canal. This suggests a right cerebellopontile angle tumor." There was a choking of the optic disks measuring 3 diopters in each eye. In spite of the negative serologic report, a diagnosis of cerebrospinal syphilis was made. The patient was transferred to the service of Dr. William G. Spiller, and later discharged to her family physician for treatment. This patient was still living, six years after the onset of blindness. At the time of this study, she walked only with support. There was marked ataxia of both upper and lower extremities. The optic disks were dead white. There was no choking. There was a complete paralysis of the right seventh nerve. The corneal reflexes were absent. There was a marked spontaneous nystagmus. In order to communicate with her, it was necessary to spell out words on the patient's right palm, using her left index finger to draw the letters. In view of these observations there was small room to question the diagnosis of bilateral acoustic tumors in this patient. She was the mother of two children—one aged 6 years and the other 18 months. These children were not examined.

V A 4, a woman, aged 32, had no suggestive history except for an occasional tendency to stagger. She denied the presence of nodules on the skin. The corneal reflex on the right was slightly sluggish. The remaining cranial nerves were normal. The Bárány test on turning and douching precluded the possibility of acoustic tumor.

To the next member of this fifth generation, V A 5, is due a great deal of credit for the results of this investigation. He was an exceedingly able and intelligent person in view of the meager opportunities which life had afforded him. His influence made possible many of these examinations which otherwise could not have been made. He was 30 years of age. He was married and the father of three children ranging in age from 6 months to 6 years. None of the latter was examined. He first noticed that he was completely deaf in the right ear at the age of 14. This was called to his attention during a routine examination at school. There was no history of discharge from the ears. He had noticed tinnitus since the age of 15. For the past few years it had been present only in the left ear. Deafness in the left ear began at the age of 16 and was slowly progressing. For ten years there had been spells in which he suddenly became completely deaf and remained so for from three to seven days with gradual recovery. These occurred from every one to three months. He occasionally suffered from headache, which he found could be relieved by taking epsom salts or a preparation of bromine. There had been no vomiting, no vertigo and no staggering, although the subject stated that sometimes when he stumbled he did not regain his balance as quickly as he should. On examination there were no positive cerebellar signs. There was a slight impairment of the corneal reflex on the right. There appeared to be an entire absence of hearing in the right ear with a marked diminution of hearing in the left. An audiogram disclosed a hearing loss of 93.5 per cent on the right side and 57.2 per cent on the left. The cranial nerves otherwise appeared normal. There was no choking of the optic disks. An examination of the nose and throat by Dr. James A. Babbitt revealed a nasal septum markedly deviated to the right with a firm synechial attachment, over 1 cm. in length, between the septal ridge and the right wall of the nose. Dr. Pancoast's report on the roentgenograms of the skull was as follows: "There is no evidence of increased intracranial pressure. The pituitary fossa is within normal limits of size anteroposterior, 10 mm.; depth, 9 mm. There is a distinct deformity of the inner

portion of the right petrous bone and possibly of the left" (figs. 14 and 15). A Bárány examination was performed by Dr. Lewis Fisher, who found that there was an entire absence of vestibular responses with the exception of a very poor response from the left horizontal canal. In view of these observations, together with the family history, there was little room to doubt that this man had bilateral acoustic tumors.

V A 6 was studied on the neurosurgical service of the University Hospital, and his record has already been given. This was the patient whose family history stimulated this investigation.

V A 7, a sister of the aforementioned patient, was deaf and blind when she died at the age of 26. On April 18, 1928, she was admitted to the Danville State

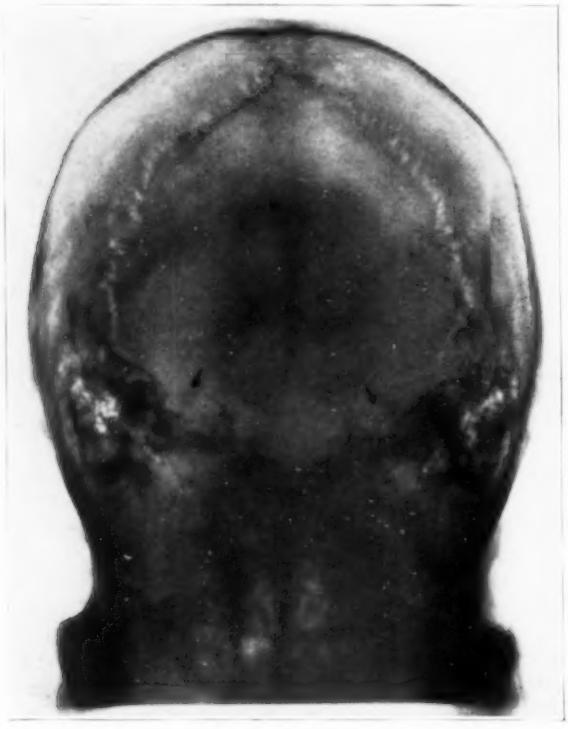

Fig. 14.—Patient VA 5. The arrows indicate the deformities of the petrous bones.

Hospital, from which a record was obtained through the courtesy of Dr. J. A. Jackson, superintendent. At the time of admission, it was impossible to obtain any information from her, as she was apparently deaf, dumb and blind. From the sister the following history was obtained: The patient had been blind for about six months and deaf for about three years. Early symptoms were staggering and loss of hearing. She complained of headache and pains in the legs. For four months she had had hallucinations of persecution. She had not been able to feed herself since the onset of blindness.

On examination, the patient lay in a stupor, unable to speak or reason or to help herself in any way. She exhibited athetoid movements of the hands. Her

speech was thick, and it was impossible to understand anything she tried to say. The pupils of the eyes did not react to light. There was difficulty in swallowing due to paralysis of the fauces. The face had lost its expression. She had chronic conjunctivitis, and the eyelids only partially covered the eyes. There was a beginning corneal ulcer at the lower corneoscleral junction of the right eye. The left eye was less congested than the right. The pupils were unequally dilated, the right being larger. They were irregular and immobile. Examination of the fundus of the right eye revealed the arteries diminished in size, the outline of the disks not sharply defined and evidence of subsiding optic neuritis. The

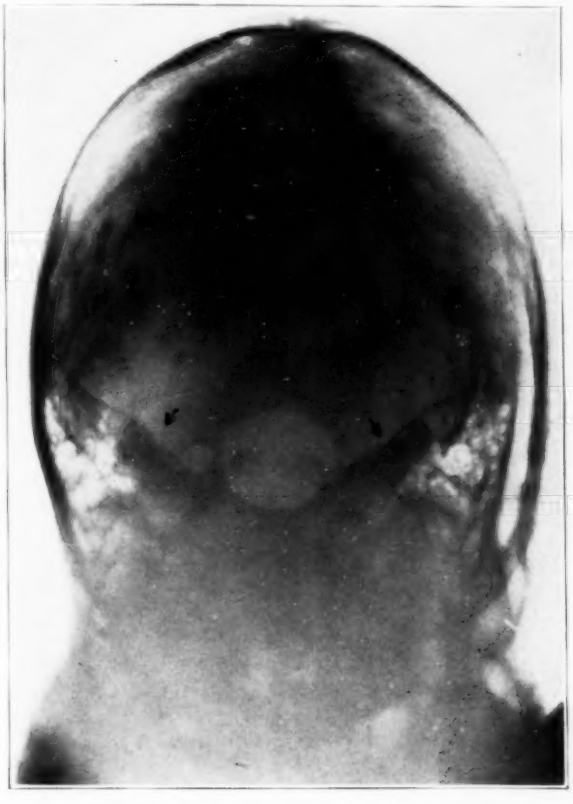

Fig. 15.—A normal roentgenogram for comparison.

left eye revealed marked optic neuritis. The patient was totally blind. The left patellar reflex was absent, and the right was very sluggish. There was no Babinski sign or ankle clonus. The Wassermann reactions of the blood and spinal fluid were negative. The patient became progressively weaker during her stay in the hospital, and died on July 26. The cause of death was given as tumor of the brain. At necropsy, the brain was removed in the usual way. A slight increase in the amount of cerebrospinal fluid was found. The veins were moderately full, but the arteries were apparently normal. No evidence of any gross lesion was found, and the membranes were not adherent to the cortex. On removal of the brain and examination of the base, two symmetrically placed

tumors were found in the pontile angles. The right was 1½ inches (3.8 cm.) in diameter, and the other a trifle smaller. They were enucleated with the finger without any difficulty. The only attachment appeared to be vascular. A cross-section of the brain revealed no pathologic condition macroscopically. On July 28, 1928, Dr. Kenneth Fowler, of the Geisinger Memorial Hospital, presented the following pathologic report: "The specimen (removed from the cerebellopontile angle) on gross examination is an hemispherical mass of fairly firm

Fig. 16.—Patient VA 7. Fibrous bands with interspersed areas of a looser reticular nature. Definite palisading of nuclei is evident. Hematoxylin and eosin; × 160.

grayish tissue, about 4 cm. in diameter. The cut surface shows a radiating structure. On microscopic examination the tissue is found to be composed of fibrous cells with abundant stroma. No nervous elements are seen. Diagnosis: cerebellopontile angle tumor (probably similar to tumor of nervus acusticus, Cushing)." Figures 16 and 17 are photomicrographs of this material.

V A 8, a woman, aged 24, gave no history suggestive of acoustic tumor. She stated that she had no skin nodules over her body, and none were visible. The

cranial nerves appeared to be normal. There was perhaps a slight impairment of hearing in testing with a high-tone fork. There were no positive cerebellar signs. The Bárány reactions on turning and douching were practically normal.

V A 9, a man, aged 21, had noticed tinnitus on three occasions in both ears within the past few years. These attacks lasted for only a few minutes. He had no other history suggestive of acoustic tumors. He denied the presence of any skin nodules. His cranial nerves appeared to be entirely normal. The audiom-

Fig. 17.—The same field shown in figure 16; × 627.

eter examination revealed a loss of hearing of 24.1 per cent in the right ear and of 30.5 per cent in the left ear. This patient was also examined by Dr. James A. Babbitt, who reported a much retracted Schrapnell's area in each tympanum with a deflection of the nasal septum to the right and a firm synechial attachment to the right wall of the nose.[20] The eyegrounds appeared normal.

20. This condition was mentioned also in the case of this subject's brother, V A 5.

The Wassermann reactions of the blood and spinal fluid and the reaction to the colloidal gold test were negative. The spinal fluid pressure was 200 mm. of water. Roentgenograms of the skull by Dr. H. K. Pancoast were entirely normal. Dr. Lewis Fisher performed the vestibular examination which disclosed that the semicircular canals were nonfunctioning, with the exception of the left horizontal canal, and the response from that canal was considerably diminished. On a little closer questioning, the patient stated that he staggered a little at times, especially at night. The diagnosis in this case was bilateral acoustic tumors in a very early stage of development.

V A 10, a girl, aged 19, was free from symptoms, according to reports. She was inaccessible for examination.

Therefore, in summing up the histories of the children of V A, we find that of a total of ten one died at the age of 7 and another was not available for examination. Of the remaining eight, two died deaf and blind and at necropsy were found to have bilateral acoustic tumors. One daughter who was deaf and blind was still living. One son was living who was quite deaf. Another son was living whose markedly impaired vestibular responses suggested a diagnosis of early acoustic tumors. The oldest son showed no response on stimulation of the vertical semicircular canals. Two daughters were apparently free from any suggestion of the disease.

V B, to revert again to the fourth generation, was a man, aged 64 (fig. 13), who had no history suggestive of acoustic tumor. His voice was slightly husky, and the soft palate deviated to the right. With these exceptions, his cranial nerves appeared to be normal. The Weber test was lateralized to the right. This was found to be due to impacted cerumen. The vestibular reactions on turning were normal. He had no children.

Three members of this fourth generation died in infancy (V C, V E and V F).

V D, a man, aged 56 (fig. 13), gave a negative history. The corneal reflex on the right was markedly, and on the left moderately, diminished. His cranial nerves were otherwise normal. The ear drums appeared perfectly normal. The hearing in both ears was normal to the tuning fork test. When the ears were douched with cold water all vestibular responses were absent. The diagnosis was bilateral acoustic tumors in a latent stage of development. This man was the father of eleven children ranging in age from 6 months to 22 years, none of whom was examined. It is reported that none of them had any impairment of hearing.

In V G, a woman, aged 53 (fig. 13), the following history was considered as slightly suggestive of acoustic tumor: She had had occasional dizzy spells for "quite a while." She occasionally staggered and had difficulty in walking after dark. She stated that she had a "light stroke," twenty years ago, affecting the right side of her face. This cleared up within two weeks. There was a soft pedunculated nodule, 0.5 cm. in diameter, on the left cheek, but the subject denied the existence of any other skin nodules. Her father died of diabetes. The patient herself had had diabetes for ten or twelve years. Examination of her cranial nerves gave negative results, except for a slight hypalgesia in the second division of both fifth nerves with an absent corneal reflex on the right and a sluggish corneal reflex on the left. The vestibular reactions on turning and douching were sufficiently active to exclude the diagnosis of an acoustic tumor. The Wassermann reaction of the blood was negative. This woman was the mother of eight children ranging in age from 18 to 34 years, two of whom were available for examination:

V G 4, a man, aged 27, gave no history suggestive of acoustic tumors. There were no skin nodules present on the visible portion of his body, and he denied their presence elsewhere. Examination of the cranial nerves gave entirely negative results. The ear drums appeared normal. The Wassermann reaction of the blood was negative. The Bárány reactions, though markedly subnormal, did not suggest the presence of an acoustic tumor.

V G 8, a man, aged 18, gave no history suggestive of an acoustic tumor. The cranial nerves were entirely normal. There were no positive cerebellar symptoms, and the Bárány reactions on turning were normal.

V H, a woman, aged 49, had an unimportant history (fig. 13). The cranial nerves were normal. There were no positive cerebellar signs, and vestibular examination on turning revealed no abnormality. She was the mother of two children, aged 25 and 27, who were not available for study.

V I, a woman, died deaf and blind. She had no children. No further information concerning her was elicited from members of the family.

V J, a woman, aged 56 (fig. 13), was completely deaf and was the mother of four children, one of whom was also deaf. Her history was as follows: Deafness began at about the age of 26. Tinnitus probably started after the deafness. She began to lose hearing in the right ear first. She was in an automobile accident at the age of 44 in which she sustained a fractured nose and following which the left eye became bloodshot. She was not unconscious after the accident. For two weeks afterward, the left side of the face and both sides of the chin were numb. She believed that the tinnitus commenced after this accident. She had always been subject to headaches, but showed improvement. She complained of an occasional heavy feeling in the occiput. There was no history of vomiting. Vision was unimpaired. She had complained of dizziness and staggering for seven years. There had been no discharge from the ears. On examination, she presented a firm swelling, 2 cm. in diameter, over the right olecranon which was adherent to the bone. This was not painful or tender. She denied the presence of skin nodules elsewhere. Examination of the cranial nerves yielded the following data: There was no choking of the optic disks. The pupils were normal in size, equal and regular. They reacted normally to light and in accommodation. The ocular rotations were full. There was hypalgesia in the distribution of the right fifth nerve with a sluggish corneal reflex on the right. In testing with the tuning fork and the loud voice, the subject seemed to be entirely deaf in both ears. Her voice was loud and monotonous. In the Romberg test she swayed in all directions. The gait was slightly ataxic, and she tended to stagger to either side on attempting to walk. There was no spontaneous nystagmus. The Wassermann reaction was weakly positive. There was no response obtainable from either vestibular nerve on turning or douching. Roentgenograms of the skull revealed a suspicious erosion of the posterior surface of the inner portion of the right petrous bone. The diagnosis was: (1) bilateral acoustic tumors and (2) syphilis.

All four sons of the foregoing subject were examined: The first, V J 1, was free from all symptoms.

The second son, V J 2, aged 37, was almost completely deaf, but could hear a little with the left ear. He first noticed, at the age of 16, a hissing in the right ear similar to that of escaping steam. About two years later, it started in the left ear. Loss of hearing began after the hissing. He could hear to talk over the telephone until the age of 23. Deafness had been steadily increasing. At the time of this investigation, the right ear was completely deaf, and the subject could hear only the very loud voice in the left ear. Tinnitus was still

present in both ears. There had never been any discharge from the ears. There was one small skin nodule below the left nostril which had been present for the past year. It measured about 0.5 cm. in diameter. It was increasing in size, but was not tender or painful. The patient denied the presence of any other skin manifestations. He stated that he had had a Wassermann examination of the blood which was reported negative. Examination disclosed cataract in the left eye, no choking of the right optic disk, a slight left external strabismus and bilaterally sluggish corneal reflexes. Hearing was apparently absent in the right ear. The patient could hear the vibrations of the 64 fork at one-half inch (13 mm.) in the left ear. He did not hear the higher tones. The ear drums appeared normal. There were no positive cerebellar signs. The vestibular responses on turning and douching were entirely absent, with the exception of a questionable response of the left horizontal canal. Roentgenograms of the skull showed a suggestion of erosion of the inner portion of the posterior surface of the right petrous bone. The diagnosis was bilateral acoustic tumors. The son of this man was examined and found to be free from any suggestion of acoustic tumor. He was 13 years of age. As he was a member of the sixth generation, he was not included in this report.

V J 3, a man, aged 34, had an unimportant history. His cranial nerves were entirely normal. There were no positive cerebellar signs, and the vestibular reactions on turning and douching were normal. He was the father of two children, aged 12 and 13 years, who were not examined.

V J 4, a man, aged 32, had no symptoms suggestive of acoustic tumor, except that he was a little unsteady on his feet after dark. On examination the cranial nerves were found to be intact. There were no positive cerebellar signs. The ear drums appeared normal. When the right ear was douched, no response was obtained from the vertical canal after four minutes. The response from the right horizontal canal was very sluggish. The patient at this point refused to cooperate further in the examination. Right-sided acoustic tumor can probably be excluded from the diagnosis.

The next member of the third generation, VI (fig. 13), was a man who died at the age of 49. He was born in 1843 and took part in the Civil War. On returning from the war he began to become deaf. This deafness was slowly progressive, but the age at which it became complete was not known. For one year prior to death, he was blind and had severe headaches. He had no children.

VII, a man, who also died at the age of 49 (fig. 13), was completely deaf for five or six years and blind for about one year prior to death. He complained of moderate headaches. He was the father of ten children.

VII A, a man, aged 57 (fig. 18), complained of no symptoms suggestive of acoustic tumor. His cranial nerves were apparently normal. There were no positive cerebellar symptoms. He refused to cooperate in the Bárány test. He was the father of five children, two of whom died in infancy. The remaining three were not examined. Their ages ranged from 18 to 29 years. According to their father, none of them was hard of hearing.

VII B, a girl, died at the age of 23 of tuberculosis. VII C died in infancy.

VII D, a woman, aged 55, complained of no symptoms suggestive of acoustic tumor except for a very occasional tinnitus. She was the mother of seven children ranging in age from 15 to 33 years. None of these children was examined. On examination this subject was found to have cranial nerves intact except for bilaterally absent corneal reflexes. The hearing was normal to the tuning fork tests. The ear drums appeared normal. There were no positive cerebellar signs. The station and gait, however, could not be tested because of a recent

fracture of the hip. No vestibular response could be obtained on caloric stimulation of either side. The diagnosis was bilateral acoustic tumors in a latent stage.[21]

VII E died of diabetes at the age of 46 (fig. 18). He was said to have been unaffected. He had no children.

VII F was said to have been affected. She died at the age of 32. She was paralyzed on one side and was totally deaf for a number of years prior to death. She also had no children.

VII G, who also died at the age of 32, was said to have been deaf for three years and blind for one year prior to death. No further information concerning her was obtained. She was the mother of two children who died of pneumonia in infancy.

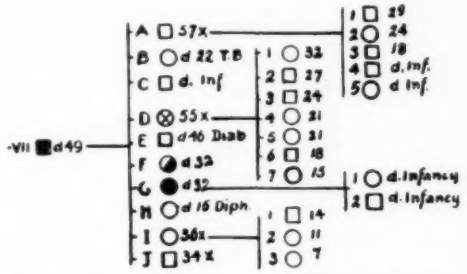

Fig. 18.—The seventh member (VII) of the third generation and descendants.

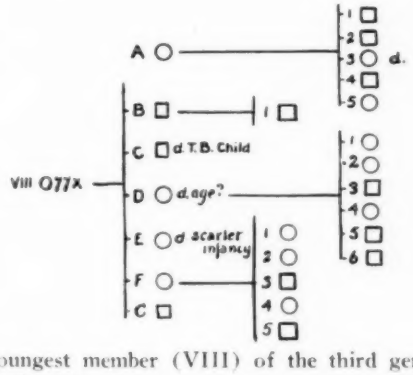

Fig. 19.—The youngest member (VIII) of the third generation and descendants. All were unaffected.

VII H was a girl who died of diphtheria at the age of 15.

VII I, a woman, aged 36, was the mother of three children ranging in age from 7 to 14 years. These children were not examined. She complained of no symptoms suggestive of acoustic tumor except an occasional tinnitus. Examination of the cranial nerves gave entirely negative results, with the exception that the corneal reflexes were bilaterally absent. The ear drums appeared perfectly

21. It is exceedingly important that the children of this subject be examined in order to determine whether this latent tendency has been transmitted. This has not been possible due to lack of cooperation on the part of the subjects.

normal and the hearing was unimpaired. There was a spontaneous past pointing of 2 inches (5.08 cm.) to the right in the vertical plane with the left hand. There were no other positive cerebellar signs. The patient denied the presence of any skin manifestations, and none was observed on the visible portion of her body. Turning to the right elicited a horizontal nystagmus of twelve seconds' duration; turning to the left, a horizontal nystagmus lasting twenty-seven seconds. At this point the patient became quite apprehensive and refused to proceed with the test. Bilateral acoustic tumors could be excluded from the diagnosis.

VII J, the youngest member of this fourth generation, was 33 years of age. He was studied completely in the neurosurgical service of the University Hospital, but exhibited no signs or symptoms which could not be explained by a chronic bilateral otitis media which had been present since the age of 23.

VIII, the youngest and only living member of the third generation (fig. 19), was a remarkable woman, aged 77. She was responsible for a considerable portion of the family history herein described. She complained of no symptoms suggestive of acoustic tumor. On physical examination she was found to have two small hard bony nodules on the scalp which were not at all suggestive of the skin nodules of von Recklinghausen's disease. She denied the presence of any skin manifestations elsewhere. She exhibited a frequent blepherospasm and had a slight impairment of hearing in the right ear. There was evidence of a chronic right otitis media. The vestibular reactions on turning were normal. She was the mother of seven children and the grandmother of seventeen, none of whom was examined and all of whom were said to be unaffected.

COMMENT

We now consider this family from the genetic standpoint. It has been shown that the hereditary make-up of individuals consists of separable units. These units are referred to as genes. The reproductive cells of the affected members of this family contain, therefore, a gene for bilateral acoustic nerve tumors which is dominant. This gene we may represent by the letter "T." If we accept the fact that all of the members of the second generation were deaf, we must assume that their paternal parent in the first generation carried a "double dose," so to speak, of this dominant gene. (This occurred in his germ plasm either by inheritance or as a mutation.) He would therefore be represented genetically as (TT). His normal wife, if such she were, would then be represented as (tt). In this case, "t" represents the normal gene. The combinations of these two pure strains would then result in hybrid offspring. (TT $\times$ tt) yields 12 (Tt) (fig. 8). Furthermore, T being the dominant gene, all members of this generation would show the defect even though they were really hybrids. If now this hybrid generation married normal persons, only half of their children would be affected. Thus, (Tt $\times$ tt) yields (Tt) and (tt) in equal numbers. Furthermore, once the dominant gene is eliminated in one branch of the family, it cannot crop up again unless there is an intermarriage with an affected member of another branch. In this respect also, this particular disease obeys the laws of Mendel as may be readily seen by

consulting the charts. There is no evidence of sex linkage or sex limitation.

The average age of onset of deafness in the fifth generation was 20 years. The age of onset in the previous generations could not be

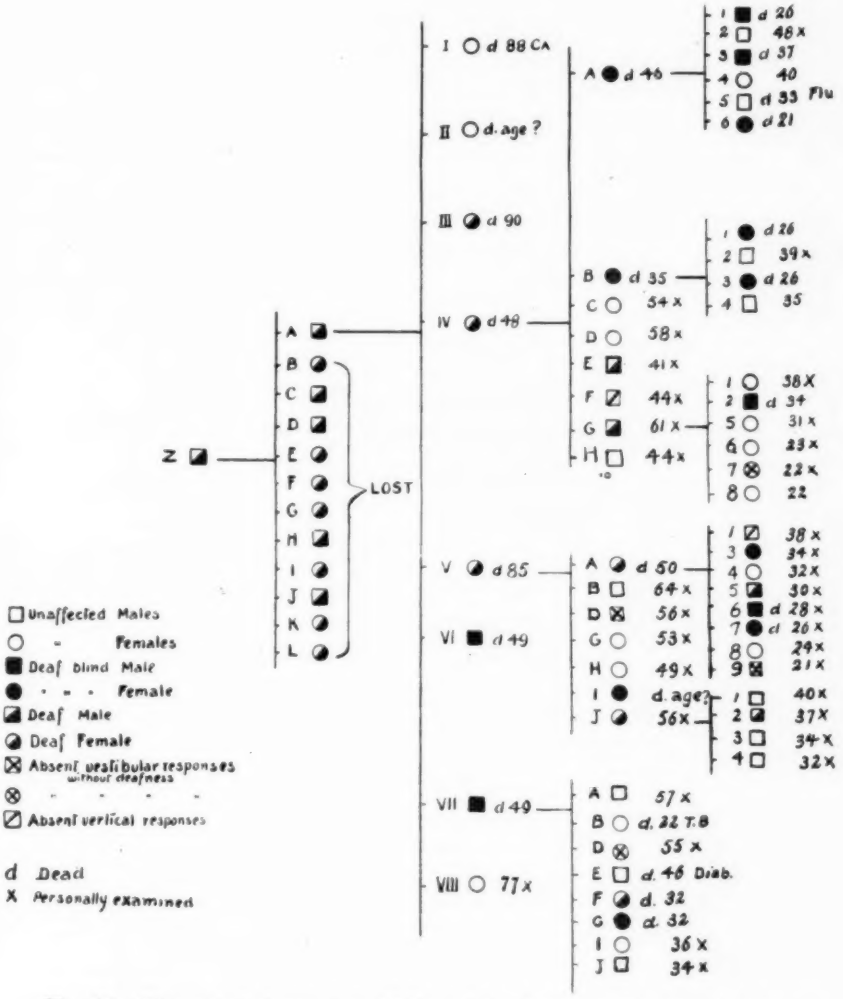

Fig. 20.—This chart shows the children of deaf parents who attained the age of 20. Only the children of affected parents were affected. The average age of onset of deafness was 20 years.

determined with any degree of accuracy. Therefore, a chart (fig. 20) was compiled which represents only the children of the affected parents who attained the age of 20 years, the average time at which the condition became manifest. The total number of members who attained the age of 20 years in the third, fourth and fifth generations was

fifty-nine; of this number, twenty-five became completely deaf. In addition, four members were found whose hearing was practically normal, but whose absent vestibular responses suggested that they had the condition in the latent stage. This made a total of twenty-nine affected members of the fifty-nine who were available and almost exactly met the requirements of the mendelian principles; namely, that half of the children of affected parents should be likewise affected if the condition is transmitted as a true dominant.

On examining the ages of the affected persons, it will be found that the only member of the second generation concerning whom we have information died at the age of 72. In the third generation, the average age at death was 64. In the fourth generation, it was 42, and in the fifth generation 28 (fig. 21). Thus it would seem that the tumors were becoming more malignant as the transmission proceeded. Hoekstra [2] stated: "Neurofibromatosis is to be considered as a systemic disease

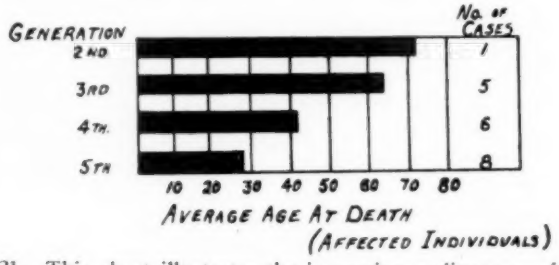

Fig. 21.—This chart illustrates the increasing malignancy of the disease.

dependent on a congenital anlage, which may be traced through as many as four successive generations during which transmission it seems to constantly increase in degree and extent."

The table gives a summary of the more important observations in the affected persons who were examined. It is curious to note that of thirteen definitely affected members, the right side was first involved in nine and the left side in three and in the remaining case there was no suggestion of laterality. The three persons in whom the left side was apparently attacked first were all of the same branch of the family. In the histories of IV G and IV G 2 it was stated that deafness began first in the left ear. In IV G 7 there was no appreciable loss of hearing, but the vestibular reactions were absent and there was impairment of the left corneal reflex. With the exception of these three cases, it would seem that the right side was affected first. IV E was quite certain that deafness began in the right ear. In V A 3, although completely deaf in both ears, there was still a suggestion of a response obtainable from the left horizontal canal at the time when she was studied at the University Hospital in 1923. In addition, there was a marked right-sided paralysis

Summary of the Observations in Sixteen of the Affected Persons

Case	Age, Years	Duration Tinnitus: Right, Years	Duration Tinnitus: Left, Years	Duration Partial Deafness: Right, Years	Duration Partial Deafness: Left, Years	Duration Complete Deafness: Right, Years	Duration Complete Deafness: Left, Years	Duration Blindness, Years	Hearing Tuning Fork Tests, Inches: Right 64	Right 256	Right 2000	Left 64	Left 256	Left 2000	Vestibular Reaction, Absent (0), Impaired (1): Horizontal Right	Horizontal Left	Vertical Right	Vertical Left	Method Turning (T) Douching (D) Both (B)	Corneal Reflex Absent (0) Impaired (1) Normal (2): Right	Left
IVE	41	?	12	?	6	23	0	0	0	0	0	0	1	0	0	0	0	0	B	1	1
IVG	61	20	20	?	?	20	20	0	0	0	0	0	0	0	0	0	0	0	B	2	1
IVG2	34	7½	8	7	7½	?	3	?	0	0	0	0	0	0	..	..	..	..	..	..	..
VA3	34	?	?	?	?	13	13	6	0	0	0	0	0	0	0	1	0	0	D	0	0
VA5	30	15	15	?	14	16	0	0	0	0	0	0	2	0	0	1	0	0	B	1	0
VA6	28	?	?	11	11	6 †	6 †	2 †	0	0	0	0	0	0	0	0	0	0	D	1	1
VA7	26	?	?	?	?	3	3	9 ‡	..	..	..	..	..	..	..	..	..	..	..	..	..
VJ	56	?	?	30	30	?	?	0	0	0	0	0	0	0	0	0	0	0	B	1	2
VJ2	37	21	19	21	19	?	0	0	0	0	0	½	0	0	0	0	0	0	B	1	1
IVG7	22	0	0	0	0	0	0	0	3	12	good	3	12	good	0	0	0(?)	not tested	B	2	1
VA9	21	3(?)	3(?)	0	0	0	0	0	3	12	good	3	12*	good	0	1	0	0	B	2	2
VD	56	0	0	0	0	0	0	0	4	12	good	4	14	good	0	0	0	0	D	1	1
VHD	55	?	?	0	0	0	0	0	4	6	good	4	6	good	0	0	0	0	D	0	0
IVE1	10	1	1	0	0	0	0	0	3	5	good	3	5	good	1	1	0	0	B	..	..
IVF	44	0	0	0	0	0	0	0	5	7	good	0*	2	poor	1	1	0	0	D	2	2
VA1	38	?	?	0	0	0	0	0	3	9	good	2	8	good	1	1	0	0	D	1	1

† Weeks; ‡ Months; * Impacted cerumen.

of the seventh nerve. These observations would seem to indicate that the larger lesion was on the right side. V A 5 was quite certain that his deafness began in the right ear. In V A 6 and V A 7, observations at necropsy disclosed that the larger tumors were on the right side. V A 9 had no appreciable impairment of hearing, but only the left horizontal canal responded to stimulation. V J stated that deafness began in the right ear first. Confirmatory evidence was found in a sluggish right corneal reflex as compared with the normal left reflex. V J 2 was quite definite concerning the earlier onset in the right ear which was completely deaf. There was still some hearing preserved in the left ear. In V D the only suggestion of lateralization consisted in a markedly diminished right corneal reflex with a moderate diminution of the left. In this case the hearing was about normal and equal on the two sides, but all vestibular responses were absent. In VII D there was no suggestion of lateralization. In the remaining three subjects indicated on the chart (IV E 1, IV F, and V A 1) there was scarcely sufficient evidence to class them as bilateral tumor suspects. It is our belief, however, that IV E 1, aged 10, with bilateral tinnitus and absent vertical responses, will go on to develop a complete loss of vestibular responses and subsequent deafness.

SUMMARY

A family of five generations and 217 members is described, in which bilateral deafness was transmitted as a mendelian dominant character. Thirty-eight members were affected. Of these thirty-eight, fifteen subsequently became blind. Of the deaf and blind persons, four were examined prior to death and were found to have choking of the optic disks with secondary atrophy. Of the deaf persons, seven were personally examined. Five of these had entire absence of vestibular responses in the Bárány test. In the other two, a sluggish response was obtained from the left horizontal canal, but the remaining semicircular canals were nonfunctioning. In addition, four subjects were found with little or no impairment of hearing, but with absent vestibular responses in the Bárány test. These Bárány observations, together with the neurologic signs which these persons presented, made the diagnosis of bilateral acoustic tumors practically indisputable. The two members of this family who came to necropsy had bilateral acoustic neurofibromas. The average age of onset of deafness was 20 years. The average age at death of affected persons in the second generation was 72; in the third generation 63 years, in the fourth 42 years and in the fifth 28 years. Therefore, the condition was increasing in malignancy as transmission proceeded. There was practically no associated evidence of von Recklinghausen's disease in this family. The results of this investigation indicate that acoustic tumors take their origin on the vestibular portion of the eighth nerve.

ABSTRACT OF DISCUSSION

DR. WILDER PENFIELD, Montreal: This is a most amazing family. Dr. Gardner was good enough to send me some of the material and some sections and I must subscribe to his diagnosis of a von Recklinghausen's disease. Of course, it is a well known fact that von Recklinghausen's neurofibromatosis is a familial disease. Its presence is often shown in one member of the family by pigmentary areas in the skin and in others by the appearance of tumors.

Here is a most remarkable family in which it affected only the eighth nerves and that bilaterally. Has Dr. Gardner found any other cases of neurofibromatosis recorded which have the familial characteristic of the appearance of tumors on one nerve or on one type of nerve? As a rule, the peripheral cerebrospinal nervous system and the sympathetic nervous system are affected.

Microscopic examination of these tumors from Dr. Gardner's patients shows wandering nerve fibers that pass through the tumor substance, which is the characteristic that makes possible a certain diagnosis of neurofibroma as distinguished from a perineural fibroblastoma of nerve or nerve root. The solitary tumors, which appear on the eighth nerve most frequently and on the spinal roots, show a histologic appearance similar to some of the sections that Dr. Gardner has shown with palisading nuclei, but the solitary tumors never, in our experience, contain nerve fibers that pass through the tumor tissue. The distinguishing characteristic between the solitary perineural fibroblastoma and the neurofibroma with perineural fibroblastic change in it is the fact that in the latter there are always nerve fibers passing through the tumor substance.

This is just further remarkable evidence that von Recklinghausen's disease is a great deal more than a case of multiple neoplasms. It is a diffuse disease affecting the nerves, and chiefly the nerve sheaths. One aspect of the disease is the tendency to the formation of secondary tumors on the nerves.

DR. RAMSAY HUNT, New York: This is certainly a most unusual series of cases. I have never encountered anything like it nor am I familiar with any similar group in the literature.

A number of years ago, I presented, with the late Joseph Frankel, cases of central neurofibromatosis with acoustic tumors. Some of them were bilateral, and others unilateral. Practically all showed other manifestations of neurofibromatosis in the skin or peripheral nervous system, although in some the indications were slight.

One thing that strikes me about the group of cases just reported is the early and high degree of deafness, which was by no means so marked in the cases of acoustic tumor that I observed.

Often, only a moderate diminution in hearing was detected and yet at the operation a large-sized acoustic tumor would be found. We interpreted this as being due to the peculiar nature of the growth, many functioning fibers persisting in the fibromatous mass so that a certain degree of hearing was preserved. It seems rather unusual that deafness should occur so early and persistently, and that it should be "stone-deafness," in so many of these cases.

It suggests the question as to whether there is not associated another pathologic anomaly in this family, in the auditory mechanism itself. It is well known how common hereditary disorders of hearing are in the otosclerotic group. It would be interesting if more of this family should come under observation and the opportunity is afforded to have the auditory mechanism subjected to careful pathologic examination.

DR. CHARLES H. FRAZIER: In going over Dr. Gardner's material yesterday, I was especially impressed with the fact that in 100 per cent of the cases there

was no indication of recognized von Recklinghausen's disease, so-called, other than these acoustic tumors, and the question came up as to whether some specific designation ought not to be given to this syndrome other than von Recklinghausen's disease. It is certain that the usual definition of von Recklinghausen's disease includes many lesions that are totally absent in this series.

A few years ago, a paper was presented by Davenport who was particularly interested in the hereditary features. He described von Recklinghausen's disease in great detail. At no time throughout this paper was any mention whatsoever made of tumors of the acoustic nerves.

Of course, it is true that from the standpoint of the pathology and symmetry of the disease and of the hereditary tendencies, it corresponds to other cases of von Recklinghausen's disease.

One of the characteristic features of the disease, which perhaps accounts for this peculiar familial tendency, is the fact that, as has been described before, there is a family resemblance in the appearance of these tumors as to location. Many cases are recorded in which the mother of a family had an unusually large tumor in a particular location, as, for instance, over the buttocks, and her descendants had large tumors in the same location.

That same principle, therefore, would seem to apply to this particular series and to account for the fact, because of its familial and hereditary tendencies, that these tumors are transmitted from one generation to another only in the acoustic nerve.

Dr. E. D. Friedman, New York: Was Dr. Gardner able, in the patients whom he had the opportunity of examining, to demonstrate other evidences of heredodegenerative disease?

Dr. W. J. Gardner: I shall answer Dr. Friedman's question first. There was no evidence of feeblemindedness in any of these persons. One member was confined to Danville State Hospital for the Insane but I doubt very much that she was really insane. She was deaf and blind.

I believe that Dr. Frazier has answered Dr. Penfield's question in regard to the bilaterality and the symmetrical distribution. Symmetrically distributed nodules in families have been called to our attention by Preisser and Davenport. The principal tumors in some families were similarly located in certain parts of the body in succeeding generations.

Dr. Hunt suggested that there may be some other reason for deafness in this family, such as otosclerosis. Several members of this family have been studied by Dr. James A. Babbitt and Dr. Lewis Fisher for such evidence, and none was found. Furthermore, all the deaf persons had absent vestibular responses. In one or two instances there was a feeble response in the left horizontal canal but from none of the other canals. This would certainly argue against the diagnosis of otosclerosis.

MUSCLE TONE IN PARKINSONIAN STATES*

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AND
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CHICAGO

The origin of parkinsonian muscular rigidity is not clearly understood. The manifest clinical differences between it and the spasticity in disease of the pyramidal tract have led to many speculative theories which in the main have produced only controversial confusion.

The simplest and most fundamental consideration, that the rigidity is dependent on the integrity of the proprioceptive arc arising in the muscle, has not been established definitely. Walshe [1] showed that intramuscular injections of procaine hydrochloride, so graded as to paralyze the afferent nerve fibers in the muscle and to leave the activity of the motor nerve fibers unimpaired, abolishes or greatly diminishes the rigidity of paralysis agitans. Voluntary movements carried out by the muscles thus rendered flaccid are of greater amplitude and speed and are less readily fatigued than similar movements carried out when the muscles concerned are still rigid. It seems, therefore, that the integrity of the proprioceptive reflex arc from the muscle is essential to the development and maintenance of parkinsonian rigidity. Ken Kuré and Titsushiro Shinosaki [2] stated that one of their co-workers, Dr. S. Araki, examined eight patients with parkinsonian rigidity and three with paralysis agitans, and observed that cocaine produced greater relaxation than did either atropine or scopolamine. They took this to mean that cocaine acted on both sympathetic and motor tone.

Few references are found in the literature to the influence of section of the posterior roots on the muscular rigidity of paralysis agitans. Obviously, this is due to the inapplicability of the procedure because of the widespread condition of the muscles. However, two cases were

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1. Walshe, F. M. R.: The Muscular Rigidity of Paralysis Agitans, Brain **47**:159, 1924.

2. Kuré, Ken; and Shinosaki, Titsushiro: Ueber den Muskeltonus, Ztschr. f. d. ges. exper. Med. **44**:791, 1925.

reported by Leriche.[3] In one of these cases, that of a man, aged 53, the fifth, sixth and eighth cervical posterior roots were sectioned. The clinical description given is poor, but includes the observation that the rigidity remained unchanged. In the second case, the fifth, sixth and eighth cervical posterior roots on both sides were sectioned. No note is found of the condition of rigidity following the operation. In the first case the tremor was diminished, and in the second the tremor was less marked at rest, but became increased on emotional disturbances. Foerster[4] stated that section of the posterior roots produced a disappearance of the rigidity of pallidal disease. We were unable to find any reference to the clinical details in his cases. In the cases reported by Leriche too few roots were sectioned to permit the use of his results as a crucial experiment. The lack of clinical details which led to Foerster's conclusion makes his published evidence inconclusive.

Walshe properly said: "Before we may finally accept parkinsonian rigidity as a true proprioceptive reflex we shall need conclusive evidence that, like pyramidal spasticity, it can be abolished by the operation of posterior root section."

In this communication, we shall describe the effects of such an operation on a patient suffering from parkinsonian rigidity: to show that the rigidity is abolished by the operation; and, by studies of the action of atropine on decerebrate rigidity, to add support to the view that a fundamental part of parkinsonian rigidity involves a proprioceptive muscle reflex arc.

A young man suffering from the sequelae of epidemic encephalitis in the form of a parkinsonian state applied to us for help. The rigidity present was so great as to make life unbearable. Despite the administration of large and sustained doses of hyoscine, he was often unable to assist himself in the simplest wants. We felt that it was justifiable to deafferent the right upper extremity in the hope that if the rigidity disappeared, subsequent muscle reeducation would give him a serviceable extremity.

REPORT OF CASE

Postencephalitic Parkinson syndrome. Section of the right cervical fourth, fifth, sixth, seventh and eighth posterior roots on Dec. 14, 1928; loss of sensation over part of the right upper extremity. Section of the right dorsal first, second, third and fourth posterior roots on Jan. 9, 1929; complete loss of sensation in the right upper extremity. Development of contracture in the right biceps, flexor carpi ulnaris and palmaris longus muscles.

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I. G., a man, aged 20, had an attack of epidemic encephalitis in 1918. He was lethargic for sixteen days but made a good recovery and attended school during the following four years. He then worked for two years until in March, 1925, when he began to develop stiffness in the right arm and leg. This was accompanied by a tremor. From 1925 until he was first seen in November, 1927, the rigidity and tremor became more marked and the left arm and leg also became involved.

In November, 1927, he presented the typical syndrome of postencephalitic parkinsonism. The tremor was coarse and became more pronounced on active movement. There was a definite cogwheel resistance on attempts to move the arms and legs passively. The facial movements on emotional stimulation were definitely impaired. There was increased salivation and increased seborrheic secretion over both sides of the face. All active movements were performed slowly. Speech was slow and monotonous. The tendon reflexes were all present, and the knee and ankle jerks were exaggerated slightly.

Course.—The patient was given hyoscine hydrobromide, $\frac{1}{100}$ grain (0.00065 Gm.) hypodermically, every three hours, and became definitely improved. Atropine or allied drugs continued to be given during the time he was at home. He returned to the hospital for further observation a year later, in November, 1928.

The general physical condition had improved considerably, but the tremor and rigidity had increased. The facies was masklike. He could flex and extend the right forearm three times in a minute, while the same movement was performed twenty-one times per minute with the left upper extremity. Fourteen of these alternating movements were performed in the first half minute. Pronation and supination were performed three times in one minute with the right upper extremity as compared with nine times per minute with the opposite extremity. The tremor in the right arm was much more pronounced and coarser than on the left side.

Operation.—On Dec. 14, 1928, under local anesthesia, a laminectomy was performed on the third, fourth, fifth and sixth cervical vertebrae. The fourth, fifth, sixth, seventh and eighth cervical posterior roots on the right side were ligated and sectioned. The administration of atropine was stopped one week prior to the time of operation.

Immediately after the operation the patient had much less rigidity in the right upper extremity than before operation. Active movements with that arm were very ataxic and coarse. He complained of a loss of position sense. The sensory examination showed a loss as illustrated in figure 1. There was evidently a wide overlap of sensation from the lower segments of the spinal cord.

Because the patient became very uncomfortable, atropine was again given on Dec. 22, 1928, and was continued until Jan. 2, 1929.

Second Operation.—On Jan. 9, 1929, again under local anesthesia, a laminectomy was performed on the seventh cervical and first, second and third dorsal vertebrae. The first, second, third and fourth right dorsal posterior roots were sectioned. Examination of the patient on January 20 showed the following condition to be present:

Passive movement of the left upper extremity produced definite cogwheel resistance. At rest, the muscles, such as the supinator longus, were flaccid, but on passive movement they became rigid immediately. When the left forearm was extended, the muscles were hard and firm. No contractures were present. Myedema was marked on the left and only occasionally present on the right.

Direct myotatic irritablity was pronounced over the left pectoral, biceps and wrist extensor muscles and could be obtained on the right over the pectoral muscles only.

On the right, passive movement did not produce any spasticity. Complete flaccidity was present in the deltoid, triceps and extensor muscles of the wrist and fingers. The same condition was present in the flexors of the fingers unless involuntary movements occurred. There were continuous involuntary movements due to contractions in the biceps, deltoid, extensor muscles of the fingers, the interossei, flexor muscles of the wrist and fingers, and in the muscles of the thenar eminence. These movements were present but less marked in the triceps

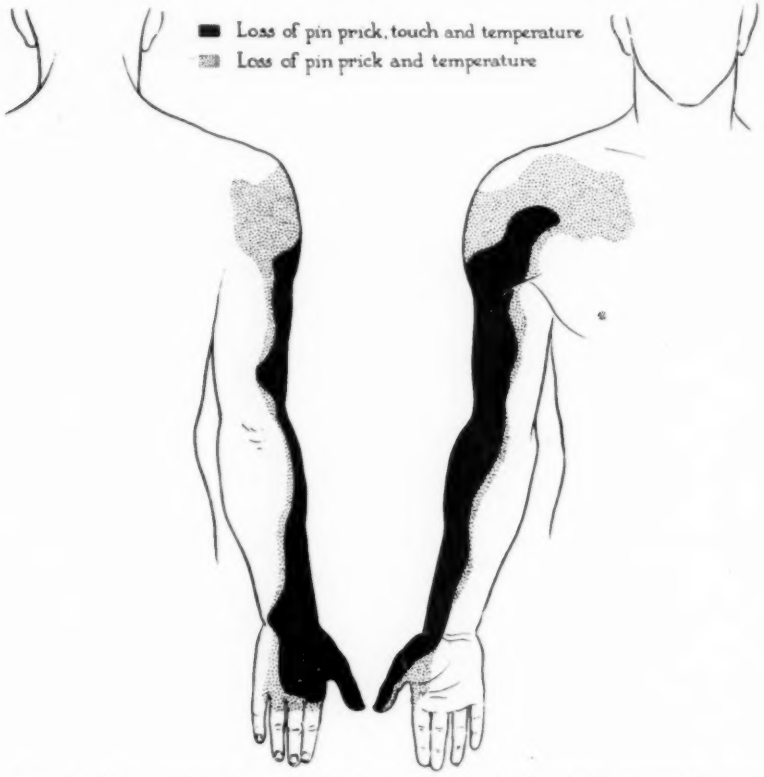

Fig. 1.—The sensory loss following section of the right posterior cervical fourth, fifth, sixth, seventh and eighth roots.

and muscles of the hypothenar group. The movements in the fingers were slow, occurring about two times per second, and were diphasic; that is, both active flexion and extension occurred. At other times, this tremor was more rapid than had been the case prior to the operation.

There was a contracture in the right biceps and in the flexor muscles of the wrist. This could be overcome only with great difficulty and the muscles were exceedingly hard and firm. Palpation of these muscles did not increase their tonicity, but stretching them beyond a certain point produced definite resistance. Passive pronation and supination on the right showed the muscles to be flaccid, whereas on the left, definite cogwheel resistance was present. Passive movement

of the right biceps muscle within an angle of 30 degrees showed complete flaccidity, but definite resistance was met with in the same movement within an angle of 60 degrees, and the muscle was found to be hard (fig. 2).

Galvanic irritability was less in the right biceps, supinator longus and flexor muscles of the wrist. The finger-nails of the left hand were pinker than those on the right. A wider area of erythema and a more diffuse flush followed scratching of the skin on the right arm than on the left. On constriction, the right arm became diffusely purplish red, remaining thus for a considerable length

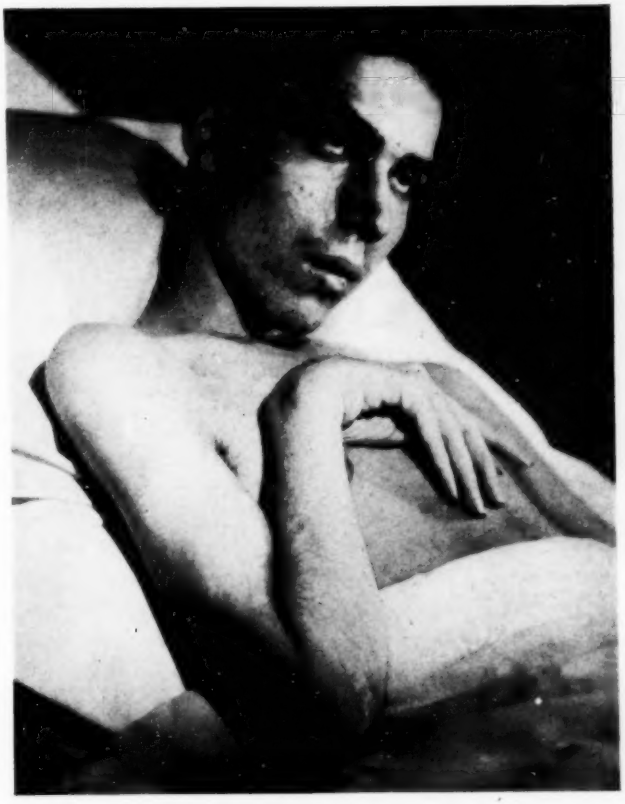

Fig. 2.—The contracture which developed in the right upper extremity of the patient.

of time after the constriction was removed. This was not true of the left arm, in which a normal reaction was present.

There was a complete loss of sensation in the entire right upper extremity, and this extended over the pectoral area as shown in figure 3.

The contracture in the right biceps muscle would relax occasionally during sleep, only to recur immediately on the first voluntary or reflex movement. The patient's head was held rigidly fixed with the chin toward the left shoulder. If the head was turned to the midline or to the right shoulder, the contracture in the biceps and flexor muscles of the wrist would relax, only to return to its full extent when the head was allowed to turn back to the left.

The right biceps muscle was given an injection of 25 cc. of a sterile 1 per cent solution of procaine hydrochloride on several occasions. No effect on the contracture was produced at any time. The administration of atropine was begun in the usual dosage without any effect on these contractures, though the usual effect was noted on the rigidity of the rest of the bodily musculature.

The patient was discharged from the hospital on Feb. 25, 1929, with the same condition present, and it has persisted up to the present time.

From this clinical description it can be seen that after severance of a number of posterior roots sufficiently to prevent any overlap of

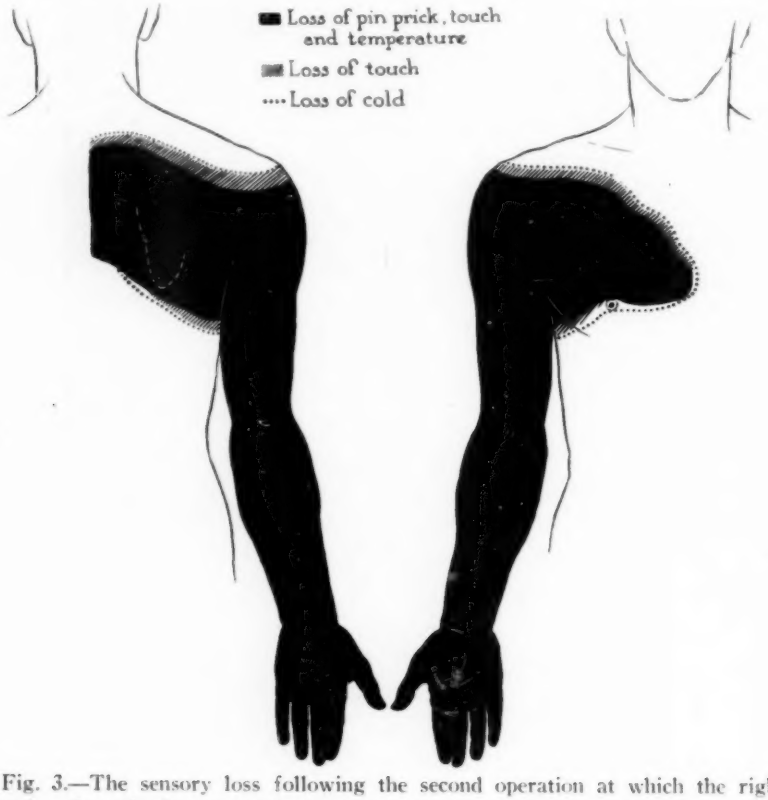

Fig. 3.—The sensory loss following the second operation at which the right posterior thoracic first, second, third and fourth roots were sectioned.

function, parkinsonian rigidity in the corresponding extremity was abolished. The tremor continued, but it was modified in rhythm and amplitude, and a secondary contracture developed only in certain muscles.

MUSCULAR RIGIDITY

The operation in this case fulfilled the requirements noted by Walshe. Does it actually lead to the conclusion that parkinsonian rigidity is a true proprioceptive reflex? It is accepted generally, after

Sherrington, that the rôle of the dorsal roots in the maintenance of tone is found in their contribution to the proprioceptive reflex arc. Recently, however, the possibility of an antidromic conduction of tonic impulses in the dorsal roots has been proposed by Frank,[5] who believed that antidromic conduction along the dorsal root fibers causes the slow tonic contraction which he regarded as the basic factor in muscle tone. Before him, von Trzecieski [6] thought that antidromic impulses traveling over the dorsal roots inhibit the relaxation of muscle and thus hold it in a state of contraction.

Liljestrand and Magnus [7] found that intramuscular injections of small doses of procaine hydrochloride greatly decrease decerebrate rigidity without abolishing the neck or labyrinthine reflexes. They attributed this to a block of the sensory impulses from the muscle. They explained their results in terms of the proprioceptive reflex theory of tonus. Ranson,[8] commenting on their observations, stated: "These results could be just as easily explained by the theory of antidromic conduction of tonic impulses along sensory fibers which would be blocked at the same time as the sensory impulse." Ranson likewise found that while section of the dorsal roots does not prevent the development of decerebrate rigidity, it deprives the condition of one of its chief characteristics, namely, plasticity. Of this he said, "According to the theory of muscle tonus that one holds, one can explain this plasticity as a steady reflex contraction called forth by afferent impulses from the tonic muscles themselves, or as due to special tonic impulses traveling antidromically over the dorsal roots." This assumption, thus far, is purely speculative, and positive proof in other directions is necessary to lend support to such a hypothesis. Recently, Ranson [9] said that in the last five years he and his associates have been engaged in putting the hypothesis to the test in a variety of experiments. "Although we have accumulated considerable data bearing upon the problem we have found no convincing evidence in favor of Frank's hypothesis."

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8. Ranson, S. W.: The Rôle of the Dorsal Roots in Muscle Tonus, Arch. Neurol. & Psychiat. **19**:201 (Feb.) 1928.

9. Ranson, S. W.: The Parasympathetic Control of Muscle Tonus, Arch. Neurol. & Psychiat. **22**:265 (Aug.) 1929.

It is not desired to enter into any discussion of this controversial problem at this time further than to say that in our experiments all the effects of residual tonicity following deafferentation of an extremity in an animal can be explained on the basis of reflex activity initiated from other parts of the body. In man, widespread resection of the posterior roots for pain in the absence of disease of the nervous system is not followed by increased tone, but by hypotonicity. Finally, the failure of section of the posterior roots, particularly when the whole extremity is not deafferented, to relieve spasticity due to disease of the nervous system does not invalidate the theory of the proprioceptive reflex arc. The recently published attractive theory of Byrnes [10] that the muscle spindle is an organ from which afferent inhibition is excited, and when this organ is diseased, as he has found it to be in paralysis agitans, rigidity occurs, does not, of course, affect the conception of a proprioceptive reflex as the basis of some types of muscle tone.

TREMOR

While this study is concerned chiefly with rigidity and while no extensive study has been made of the tremor, a few comments will be made on our observations. Byrnes attributed the occurrence of both the muscle rigidity and the tremor to disease of the muscle spindle. He believed that the tremor is the result of early changes and that the rigidity is the result of complete and widespread destruction of the spindle and progressive extinction of peripheral inhibition. Walshe, however, contended that tremor is unaffected by deafferenting the tremulous muscles and must therefore be a proprioceptive reflex. Byrnes objected to this on the basis that it is not possible by means of a local injection to deafferent completely the spinal center of a muscle or a group of muscles.

In our case, however, the entire extremity was deafferented. It was noted that although the tremor was not abolished it was changed in amplitude, rhythm and rate. Whereas prior to the operation it was slow and regular and the movements were of small excursion, following the operation they were irregular, at times more rapid and at times slower than formerly, and they frequently had an amplitude not seen in cases of parkinsonism. We do not attempt to explain this further than to note that all movements are of greater amplitude in the deafferented limb of an experimental animal, whether decerebrate or otherwise normal. It would appear that section of the posterior roots destroys the facility of a type of inhibition that affects not only the amplitude of movement, but the rhythm and frequency as well. It is

10. Byrnes, C. M.: A Contribution to the Pathology of Paralysis Agitans, Arch. Neurol. & Psychiat. **15**:407 (April) 1926.

as if by this inhibition certain refractory phases are produced which permit only a certain number of tremors to appear in a given time.

CONTRACTURE

As noted in the clinical description, a contracture occurred in the biceps, flexor carpi ulnaris and palmaris longus muscles. Little is known as to the causes of such changes in muscles which are observed under diverse conditions. They occur in muscles poisoned by tetanus toxin and shortened after the severance of tendons, after immobilization by casts and because of the unopposed action of antagonistic muscles. Ranson noted permanent shortening in the muscles of deafferented limbs of animals a week or two after operation. We have been unable to find any record of such contractures occurring after section of the posterior roots in many patients for the relief from pain not due to neurologic disease.

Dr. Ernest Sachs has permitted us to quote the unpublished case of a man, aged 44, in whom a diagnosis of paralysis agitans had been made and on whom he operated. He sectioned the sixth, seventh and eighth cervical and the first dorsal posterior roots. The history and clinical observations were somewhat atypical, and we feel that the observations as to tone are probably not admissable for the purpose of studying parkinsonian rigidity.

> The patient developed what he thought to be writer's cramp in the fingers of the right hand in 1923. This cramp then rapidly affected the wrist, forearm and arm. On July 31, 1924, when he entered Dr. Sidney Schwab's service there was marked wasting of the right upper extremity. A continuous tremor was noted in the right upper extremity. The fingers were flexed into the palm. He complained of pain in the right upper extremity and of numbness in the right leg. He was operated on, on Nov. 18, 1925. Sensory examination after the operation showed a complete loss of sensation over the hand and forearm. He was discharged on Dec. 16, 1925, and readmitted to the hospital on April 26, 1926, when he stated that a contracture of the hand and arm had begun in January, 1926. This was accompanied by pain of a pulling character. On April 27, 1926, sensations of touch, pain and temperature were lost over the seventh and eighth cervical segments anteriorly, while sensations of pain and temperature only were lost over the sixth cervical and first dorsal segments posteriorly. All sensation was lost over a part of the sixth, seventh and eighth cervical and first dorsal segments. The upper extremity was shaking and twitching. The contracture persisted, and in August, 1926, pain recurred in the hand.

In this case, then, a lasting contracture developed after section of the posterior roots. The occurrence of a contracture in our case as well indicates that it is the result of conditions not found in the muscles of persons who are not suffering from disease of the nervous system. Obviously the contracture was not the result of any sustained peripheral stimulus. It was not the result of any hypothetic antidromic tonic

impulse traveling over the posterior root distal to the ganglion; otherwise it would have disappeared following the injection of procaine hydrochloride into the affected muscle. It was not the result of a mechanism similar to that which produced the original rigidity, as it was not affected by the administration of atropine, whereas the rigidity of the opposite upper extremity was always diminished by this drug. It is significant that the contracture occurred only in certain muscles, and these were the ones usually influenced by tonic neck reflexes. In animals, we have found constantly that when a limb was completely deafferented, reflex activity in that limb produced by movement of the head, by suddenly raising the body and by many passive movements of other parts appeared uninhibited. The rigidity of the neck was marked in our case, and it is possible that unopposed neck reflexes acting on diseased muscles may have been responsible for the contracture. It is notable that the contracture during the first six weeks always disappeared in sleep when the other muscles were relaxed.

ACTION OF ATROPINE

On Decerebrate Rigidity.—Another approach to the nature of the rigidity is afforded by the study of the effect of atropine, which has a specific action on parkinsonian rigidity and decerebrate rigidity.

The favorable action of atropine and allied drugs on parkinsonian rigidity is well known. The manner in which they bring about this effect is unknown. Little has been written on the effect of atropine and similar drugs on skeletal muscles. Atropine has been called "the curare of smooth muscle." A few of the observations concerning the known action of atropine on certain types of rigidity, chiefly contractures, may be mentioned. Riesser and Neuschlosz [11] stated that the prolonged shortening of a frog's gastrocnemius muscle by immersion in a solution of nicotine or acetylcholine is prevented by atropine. Frank, Nothmann and Hirsch-Kaufman [12] found that contracture following the injection of acetylcholine into the blood stream was antagonized by large doses of scopolamine (up to 15 mg.). Hinsey [13] found that the injection of 2 mg. of scopolamine hydrobromide had no effect on acetylcholine contracture. Schäffer [14] found that Tiegel's contracture is inhibited

11. Riesser, O., and Neuschlosz, S. M.: Ueber den Mechanismus der durch giftebewirkten Kontractur quergestreiften Muskeln, Arch. f. exper. Path. u. Pharmakol. **92**:254, 1922.

12. Frank, E.; Nothmann, M., and Hirsch-Kaufman, H.: Ueber die dreifache motorische Innervation der quergestreiften Muscultur, Klin. Wchnschr. **1**:1820, 1922.

13. Hinsey, J. C.: Further Studies on the Sherrington Phenomenon, to be published; quoted by Ranson (footnote 9).

14. Schäffer, H.: Beitrage zur Frage der autonomen Innervation des Skelettmuskels, Arch. f. d. ges. Physiol. **185**:42, 1920.

by atropine. Bremer [15] called attention to the elective sensibility of neuromuscular contracture in brown frogs to atropine and scopolamine. In his experience, normal mammalian muscles did not exhibit neuromuscular contracture. Neither did the rigid muscles of patients with Parkinson's disease. He believed, with Walshe, that this rigidity is probably a reflex hypertonia and that its sensibility to scopolamine may be explained by a central action of the drug. Kuré and Shinosaki [2] stated their belief that atropine paralyzes some hypothetic parasympathetic fibers ending in skeletal muscles. Hugget and Mellanby [16] were unable to affect the tonus of intact anesthetized cats or of decerebrate animals by the injection of 5 mg. of atropine. Bremer did not believe that neuromuscular contracture is related to decerebrate rigidity of mammals, contrary to the opinion of Riesser and Simonson.[17]

In the course of some former work we were unable to affect the rigidity of decerebrate cats by the injection of from 1 to 2 mg. of atropine. It was felt that since it had been observed in parkinsonian rigidity that it was necessary at times to administer hyoscine for a day or two before its full effect was noted in untreated patients, the experiment should be repeated and should be modified by first atropinizing the animal and then performing the decerebration. Accordingly a cat was given 2 mg. of atropine hypodermically three times a day for four days and was then decerebrated by the anemic method.[18] During the four days of the administration of atropine, aside from the difficulty in vision and the increased thirst, nothing abnormal was noted in the behavior of the cat. Following this experiment, nine other animals were subjected to the same procedure, and the results were constant in all.

In sharp contrast to the normal decerebrate cat (fig. 4), it was seen that when the animal was placed on its back, the hind legs fell into a flexed position. When passively extended and allowed to fall, the limbs quickly returned to their original position without resistance. No extensor tone could be developed by pressure against the pad of the hind paw; in other words, the positive supporting reflex (Stütz) was absent. The hind legs exhibited markedly lessened tone. That this was not due to a central action was easily determined by the conserva-

15. Bremer, F.: The Tonus and Contracture of Skeletal Muscles, Arch. Surg. **18**:1463 (April) 1929.

16. Hugget, A., and Mellanby, I.: The Influence of the Sympathetic, Parasympathetic and Somatic Systems of Nerves on the Tonus of Muscles in the Intact and Decerebrate Cat, J. Physiol. **60**:8, 1925; ibid. Proc. Physiol. Soc.

17. Riesser and Simonson: Arch. f. d. ges. Physiol. **202**:221, 1924; quoted by Bremer (footnote 15).

18. Pollock, L. J., and Davis, L.: Studies in Decerebration: I. A Method of Decerebration, Arch. Neurol. & Psychiat. **10**:391 (Oct.) 1923.

tion of pronounced neck and labyrinthine reflexes acting on the hind legs and fore legs, by very active knee jerks which did not, however, manifest a stepladder effect, and by good pinna and phlyctenular reflexes, crossed extensor thrusts and withdrawal reflexes. These questions arose: Why apparently were the hind legs alone affected? What was the manner of the action of the drug? Did the drug act on the tonic neck and labyrinthine reflexes and on body-reflexes acting on the body (fig. 5)?

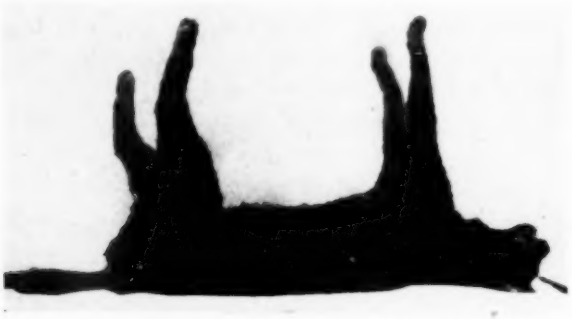

Fig. 4.—A normal cat decerebrated by the anemic method. Note the strong extensor rigidity in all four extremities.

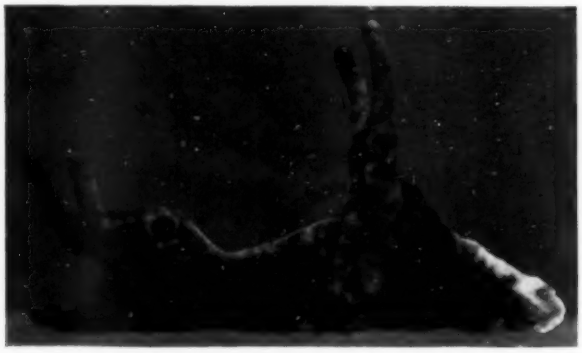

Fig. 5.—A cat which had been atropinized previous to decerebration by the anemic method. Note the flaccidity of the hind legs as compared with the strong extensor tone present in the fore legs.

Action of Atropine on the Tone of a Deafferented Extremity of a Decerebrate Animal.—Four cats were operated on. One fore limb was completely deafferented by the section of twelve posterior roots. Two weeks later, the animals were atropinized and decerebrated. The extensor tone which developed in the deafferented fore limb was less than that in a normal animal, but when a tonic labyrinthine reflex was pro-

duced by turning the occiput down, the difference in tone between the normal and deafferented limbs in an atropinized animal was only 100 Gm., whereas prior to eliciting the labyrinthine reflex, the difference was 400 Gm. The hind legs were in a position of flexion, but the fore legs were always extended. Control animals which had undergone similar operations, but which had not been atropinized, showed a similar increase of tone to labyrinthine stimulation and no less difference between the deafferented and normal extremities. This led us to feel that atropine did not affect the tonic neck or labyrinthine reflexes, and, as will be seen from further experiments, this supposition was confirmed.

Action of Atropine on the Tone of Decerebrate Animals in Which the First Four Cervical Roots Were Cut Bilaterally.—Three cats were atropinized and decerebrated three weeks after the first four cervical posterior roots were cut on both sides. These animals presented an appearance much like that of the normal decerebrate animal that was atropinized. The hind legs were flexed; they fell when passively extended and then dropped; the Stütz reflex was absent, but there were crossed extensor thrusts, and withdrawal reflexes were present. The fore legs were rigidly extended and a good labyrinthine reflex was present, but the neck reflexes were absent. A control animal which was not atropinized showed good extensor tone in all extremities. This further showed that atropine did not act on the labyrinthine reflex.

We had previously observed [19] that the pattern of rigidity in decerebrate labyrinth-less animals differed from that in normal animals. We found that when such an animal was suspended with the head passively extended, marked extensor rigidity was present in all of the extremities. When the passively extended head was allowed to drop, the fore legs immediately flexed and remained so as long as the head was allowed to remain in that position. The hind legs, however, were more strongly extended. We took this to mean that the fore legs were far more influenced by the neck reflexes than were the hind legs. This, then, might explain the difference in the action of atropine on the hind legs. To investigate this further, we decerebrated four animals in which the labyrinths had been removed and in which the first four cervical roots had been cut bilaterally. Good extensor rigidity was present in the hind legs, in fact, sufficient rigidity to support the animal's weight. The fore legs, however, were slightly flexed, the claws unsheathed and, as in other labyrinth-less animals, there was marked activity of such reflexes as the swipe, withdrawal and extensor rebound. Of course, no tonic neck or labyrinthine reflexes were present (fig. 6).

19. Pollock, L. J., and Davis, L.: Studies in Decerebration: III. The Labyrinth, Arch. Neurol. & Psychiat. **16**:555 (Nov.) 1926.

We were unable to confirm the observation of Magnus [20] that the fore legs remained strongly extended. On the contrary, the fore legs tended to flex, and this was to be expected from our experiments with labyrinthless animals. It was seen from these experiments that the tonic neck as well as the labyrinthine reflexes acted strongly on the fore legs and that other reflex activities were responsible for the extensor rigidity in the hind legs. If, however, pressure was put against the foot pad of the fore limbs, an extensor rigidity could be obtained as well as in the hind legs.

Action of Atropine on Decerebrate Animals in Which the Labyrinths Had Been Removed and in Which the First Four Cervical Roots Were Cut Bilaterally.—Three such animals were prepared. All of the extremities were held in a flexed position when the animal was lying on its back. When the extremities were passively flexed further, they remained so. No Stütz reflex could be obtained from any of the limbs. Some extensor rigidity could be found, chiefly in the hind legs. When

Fig. 6.—A cat decerebrated by the anemic method after the first four cervical posterior roots on both sides had been removed two weeks previously and after the labyrinths had been destroyed. Note the flexor position of the fore legs. A definite extensor tone is present in the hind legs sufficient to support the animal's weight, and a Stütz reflex can be elicited.

the hind legs were passively flexed to an angle of 60 degrees, resistance was met. This remained at the same level throughout further flexion. Very active knee reflexes without a staircase effect were present. Marked withdrawal and contralateral thrust and swipe reflexes were present. It was evident, therefore, that when the tonic neck and labyrinthine reflexes were destroyed, atropine diminished tone in all the extremities alike (fig. 7).

In all the various preparations after the administration of atropine, body reflexes acting on the body were preserved. For example, the tone in the side lying on the table was always greater than that on the opposite side.

20. Magnus, R.: Körperstellung, Berlin, Julius Springer, 1924.

SUMMARY

It seemed apparent, therefore, that atropine did not act on the central connections between the neck, labyrinthine and nociceptive reflexes. It did not act on the muscle directly, since so many of the reflex activities were increased. It did not measurably affect the tonic neck or labyrinthine reflexes or the body reflexes acting on the body. By injecting two doses of 2 mg. of atropine subcutaneously two hours apart we have been able to produce the same effect on animals that had first been decerebrated. It is likely, therefore, that either a larger dose is required than we first used or, and this is more likely, that a longer time is necessary for the effect of atropine to develop. Only one function was constantly affected; the Stütz reflex was absent and no increase of tone could be developed by putting a muscle on stretch. The seeming selectivity of the muscles of the hind legs to the administration of atropine is due to the fact that the tone in the fore legs is maintained and influenced far more by the neck and labyrinthine reflexes, whereas

Fig. 7.—A cat decerebrated by the anemic method after the first four cervical posterior roots on both sides had been removed previously, after atropinization and after the labyrinths had been destroyed. Note the entire lack of extensor tone in any of the extremities. A Stütz reflex was absent in the hind legs.

the hind legs are maintained in rigidity in extension by other reflexes, chiefly the muscle proprioceptive reflexes.

CONCLUSIONS

1. Parkinsonian rigidity is dependent on the integrity of the proprioceptive reflex arc and disappears when the posterior roots are cut.

2. Atropine diminishes that part of the rigidity in decerebrate animals which is dependent on the muscle proprioceptive reflexes. This probably explains its well known action in diminishing parkinsonian rigidity.

ABSTRACT OF DISCUSSION

DR. I. S. WECHSLER, New York: In connection with the first part of Dr. Pollock's paper, I shall report an observation which Dr. Kaufman and I made in trying to overcome rigidities and contractures in disease of both the pyramidal and the extrapyramidal tracts.

I recall reading the statement made a long time ago by a French neurologist that to differentiate between hysterical and organic contracture, one should compress the limb sufficiently, by means of a tourniquet, to abolish the arterial pulse. If it is an organic contracture, it will gradually disappear; if it is a psychogenic or hysterical contracture, it will recede following that maneuver.

We repeated the experiment in a number of cases. Unfortunately we did not have cases of hysterical paralysis to prove or disprove the assertion, but we did have contractures in cases of disease of the pyramidal and the extrapyramidal tracts. We applied the cuff of a blood pressure apparatus to the arm and raised the pressure sufficiently to overcome the systolic pressure in the limb. After a few minutes, generally not more than two or three, the contracture of the fingers and hand would gradually disappear, so that if a certain amount of strength was necessary to overcome the contracture in order to straighten out the fingers before the pressure was put on, very much less strength was necessary afterward. We measured this in terms of pounds necessary to overcome the resistance. In certain instances, the contractured and rigid hand became limp and flaccid. That occurred in practically all cases of rigidity of the pyramidal tract such as we find in hemiplegias, and also in patients who have had these contractures for months and years.

We did the same thing with patients who had parkinsonian rigidity and contractures, and there, too, we succeeded in abolishing the rigidity. Incidentally, in the cases of parkinsonian rigidity, we also abolished the tremor by the same maneuver. The disappearance of tonus and of tremor lasted as long as the cuff was on the arm and persisted perhaps for a minute or two after the cuff was removed. Subsequently, both tonus and contracture reappeared.

We have been unable to explain the phenomenon. We have a number of theories, but actually we do not know just what happens—whether it is merely the result of the removal of blood from the parts, whether centrifugal or centripetal stimuli are abolished, or whether new ones are set up. For the present, we feel that the facts themselves are of interest and worthy of record.

In connection with the second half of the paper, I wish Dr. Pollock would dwell a little more on some of the physiologic mechanisms. We know that tonic neck reflexes are not generally found in disease of the extrapyramidal tract, but are elicited in lesions of the pyramidal tracts. I was not quite clear as to the mechanisms involved in his experiments, or as to whether by means of those experiments he can prove that the rigidity in extrapyramidal disease also depends on proprioceptive reflexes.

Dr. Pollock: Of course, tonic neck and labyrinthine reflexes appear, in normal man, in diseases of the extrapyramidal motor tract and of the pyramidal tract, and I suppose in every other kind of disease, but they are so welded into the other activities that we are unable to demonstrate them. However, if we deafferent an extremity of man or of an animal, we are able to bring out tonic neck and labyrinthine reflexes. As Dr. Ranson has pointed out, reflexes are uninhibited under those conditions and reflexes appear which would otherwise not appear. Trendelenburg showed a similar thing in pigeons, and we have made note of a similar thing.

I am not in agreement with the statement that diseases of the extrapyramidal tract do not show neck and other tonic reflexes. That is one thing our patient did show. It is simply a matter of elicitation rather than absence or presence of these reflexes in various patients.

It makes little difference as to where or how this tone originates. All that we were concerned with was the simplest mechanism involved in the sustaining of the tone which had developed. From the fact that one can destroy this tone by posterior root section, one may infer that the posterior roots are an integral part of it, and from the fact that we are able to show that atropine acts on parkinsonian rigidity by a specific action on the muscle proprioceptive arc, we feel justified in assuming that the hypertonicity in parkinsonian states is dependent on the integrity of the proprioceptive reflex arc.

THE NATURE OF VON RECKLINGHAUSEN'S DISEASE AND THE TUMORS ASSOCIATED WITH IT*

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Multiple neurofibromatosis is a condition which has long proved a fascinating study because of its bizarre and varied clinical manifestations, its familial characteristics, its rarity and the large number of unsuspected lesions of the nervous system usually disclosed by necropsy.

The case of von Recklinghausen's disease to be described is one of the rare examples of this condition involving both the peripheral and central nervous system and the meninges. It is reported not merely to add one more "interesting case" to the already large literature of the subject, but because it affords an opportunity to study the disease process itself. Further, it provides an opportunity to study the nature of the tumors which under other conditions arise from the nerves, meninges and central nervous system.

REVIEW OF THE LITERATURE

Virchow [1] divided neuromas into true and false types. He considered that a true neuroma must contain nerve tissue and nerve cells. The false neuroma he considered to be made up of connective tissue elements derived from the sheath of the nerves. Von Recklinghausen [2] noted the frequency of the association of multiple "false neuromas" with tumors of the skin. He provided the term neurofibromatosis for the condition, believing that the tumors were chiefly fibrous and arose from the connective tissue sheath of the nerves, especially from the endoneurium.

Verocay [3] subsequently refused to accept the connective tissue nature of these tumors and substituted the name neurinoma which will be

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1. Virchow, R.: Die krankhaften Geschwülste, Berlin, A. Hirschwald, 1863.

2. Von Recklinghausen, F.: Ueber die multiplen Fibrome der Haut und ihre Beziehung zu den multiplen Neuromen, Virchows Festschrift, Berlin, A. Hirschwald, 1882.

3. Verocay, J.: Zur Kenntniss der Neurofibrome, Beitr. z. path. Anat. u. z. allg. Path. **48**:1, 1910.

discussed later. Lhermitte [4] found nerve cells of a central type in a tumor of von Recklinghausen's disease and concluded that these tumors spring from displaced embryonal tissue. Both Councilman and Antoni [5] pointed out that degenerating tumor cells might easily be mistaken for nerve cells.

Hereditary factors play an important rôle in the production of the disease. Preiser and Davenport [6] (1918) reviewed the literature in an excellent study, and collected thirty cases of a familial type in which two or more members of a family were affected. The disease seems to reappear in both sexes of successive generations according to the mendelian law. It must therefore be assumed that there is a defect in the germ plasm which leads to the production of tumors of the nerve sheath, under appropriate stimulation.

Outside stimuli seem to be of secondary importance in the production of these tumors. A frequently quoted case is that of Labouvière,[7] in which a gendarme had multiple tumors about the waist in a zone that was pressed on by his sword-belt. Others have stressed the importance of the brim of the hat and the clothes as irritating factors, but against all such hypotheses is the infrequent appearance of nodules on the palms of the hands or on the soles of the feet where irritation is common. Undoubtedly, after the tumor makes its appearance, pressure irritation will augment its growth, though even here it probably has little modifying effect. Various infections and intoxicants may act as etiologic factors. Metabolic changes frequently influence the course of the disease. Pregnancy stimulates it. Puberty is apt to be associated with the first manifestations of it.

Abnormalities of innumerable kinds, which are chiefly concerned with the skin, the bones, the endocrine glands and the central nervous system have been registered. Sometimes the tumors, though diffuse, assume such large proportions as to deserve the name of elephantiasis nervorum. Helmholz and Cushing [8] collected a number of cases in which the scalp was particularly involved, it being the most frequent site for this peculiar manifestation. The cutaneous lesions of the disease have attracted the attention of dermatologists; it is often they who recognize the disease in its early stages. Frequently, the only stigmas

4. Lhermitte, J., and Dumas, R.: La ganglioneuromatose disséminée, type anatomique du syndrôme de Recklinghausen, Rev. neurol. **33**:579, 1916.

5. Antoni, X.: Ueber Rückenmarkstumoren und Neurofibrome, Munich, J. F. Bergmann, 1920.

6. Preiser, S., and Davenport, C.: Multiple Neurofibromatosis and Its Inheritance, Am. J. M. Sc. **156**:507, 1918.

7. Labouvière, J.: Considération à propos de quelques cas de neurofibromatose généralisée, Thèse de Nancy, 1899.

8. Helmholz, H., and Cushing, H.: Elephantiasis Nervorum of the Scalp, Am. J. M. Sc. **132**:355 (Sept.) 1906.

of the inherited taint are the scattered pigmentary spots, irregularly distributed over the body, varying in size from that of a pinhead to that of a large plaque and colored a light yellow, café au lait or deep brown. It may be observed that the pigmentary spots are the only evidence of the disease throughout life in some members of a family, while other members are studded with the more typical nodules. To this variety of the disease the terms "incomplete" and "abortive" have been applied.

Cushing [9] recognized the frequency of the association of bilateral tumors of the auditory nerve and "meningiomas," and he was able to collect thirteen cases from the literature. These dural tumors may be multiple or single, situated in the falx or scattered throughout the meningeal coverings of the central nervous system, as in the case of neurofibromatosis reported by Fleming and Cookson.[10] It is obvious that this is no chance association but that these tumors must be correlated in some way. The rare cases of von Recklinghausen's disease which have involved likewise the central nervous system have been well summarized by Antoni. Bassoe and Nuzum,[11] reporting such a case, pointed out scattered areas in the brain of hyaline proliferated vessel walls and perivascular fibrous tissue and other minute areas containing large polymorphous, neuroglia cells. The latter areas have been noted, not infrequently, by others and have been likened to the characteristic changes of tuberous sclerosis; this observation was especially substantiated by Bielschowsky.[12]

Cornil and Ranvier [13] pointed out a supposed resemblance between myopathy and neurofibromatosis. In each condition, according to these writers, there is an hereditary and congenital basis and the progress of each malady is fostered by traumatic or intoxicating influences.

Thompson,[14] in a thorough study of the disease, noted pseudohypertrophic lipomatosis of the muscles in a case of multiple neurofibromatosis. In the light of Pick's [15] observations this is extremely

9. Cushing, H.: Tumors of the Nervus acousticus, Philadelphia, W. B. Saunders Company, 1917, p. 214.

10. Fleming, G., and Cookson, H.: A Case of Multiple Neurofibromatosis, J. Neurol. & Psychopath. **6**:104, 1925.

11. Bassoe, P., and Nuzum, F.: Report of a Case of Central and Peripheral Neurofibromatosis, J. Nerv. & Ment. Dis. **42**:785, 1915.

12. Bielschowsky, M.: Histopathologie und Pathogenie der Tuberosesclerose, J. f. Psychol. u. Neurol. **30**:167, 1924.

13. Cornil, V., and Ranvier, L.: Manual d'histologie pathologique, Paris, Félix Alcan, 1907, p. 825.

14. Thompson, A.: On Neuroma and Neurofibromatosis, Edinburgh, Turnbull and Spears, 1900.

15. Pick, L.: Ueber Neurofibromatose und partiellen Riesenwuchs, Beitr. z. path. Anat. u. z. allg. Path. **71**:560, 1922.

interesting; he reported a case of megalocolon in a horse, showing neurofibromatosis in the splanchnic nerves that supplied that strip of intestine. Oberndorfer (1921) likewise reported a giant appendix and neurofibromatosis of the innervating mesenteric nerves.

Winestine [16] reported a case of neurofibromatosis of the pelvic and sympathetic plexuses combined with an unusual blastomatosis of the lowest rectal segment, namely, papillary adenomatosis of the mucous membrane which penetrated into the inner layer of the thickened muscle wall. Scoliosis, abnormalities of growth and irregularity in outline of bones have been observed frequently in association with the disease. It has been claimed that these abnormalities are due to dysfunction of the endocrine glands, but Lehman [17] pointed out that more likely the bone growth has been influenced by the pressure of a tumor.

Based on the foregoing observations, the giant growth of the mucosa and the muscularis of the intestines associated with neurofibromatosis, one might suppose that the abnormalities of bony growth could likewise be influenced by neurofibromatosis of the nerve supply.

REPORT OF CASE

Clinical History.—Miss G. A., aged 21, was admitted to the surgical service of the Royal Victoria Hospital on Aug. 6, 1928, complaining of difficulty in walking, deafness, impaired vision, headache and dizziness. At the age of 14 she had begun to have headaches of a mild character, which later became more severe and were accompanied by nosebleed. Because of the severity of the headaches she had to give up teaching when 17 years of age. A year later, she began staggering to the left when walking, and complained of dizziness which was frequently accompanied by vomiting. At the age of 19, she took a position as telephone operator, but was forced to give up this work on account of the headaches and increasing deafness in the left ear. Gradually the staggering became more noticeable, the dizziness and headaches more severe and the deafness more pronounced. In June, 1928, she came under the care of Dr. Hingston at St. Mary's Hospital. A diagnosis of tumor of the left auditory nerve was made and admission to the Royal Victoria Hospital advised. During the next three months, hearing in the right ear began to fail, eyesight became blurred, speech became markedly slurred and the patient failed generally.

The family history is significant perhaps in that two brothers had pigmentary areas on the skin and one sister, aged 26, was mentally retarded. Another sister died of tuberculosis at the age of 17; the remaining sister is well. The father died of stomach trouble at 58. The parents were French-Canadian.

Physical Examination.—The patient was normally developed. Over the upper part of the right arm a small, bluish, firm nodule, about the size of a walnut, was seen. She had a similar, though smaller, tumor over the sternum, and on the arms there were several smaller ones. No abnormal pigmentations of the body

16. Winestine, F.: The Relation of Von Recklinghausen's Disease to Giant Growth and Blastomatosis, J. Cancer Research **8**:409, 1924.

17. Lehman, E.: Recklinghausen's Neurofibromatosis and the Skeleton, Arch. Dermat. & Syph. **14**:178 (Aug.) 1926.

were noted, except for brownish, discolored areas due to "fire-points" which had been applied early in the disease.

She was cooperative, quick in her responses and accurate in her replies, though she tired easily and was mildly depressed. There were no delusions or hallucinations. Speech was sometimes slurred and indistinct. There was papilledema of from 3 to 4 diopters in both optic disks; vision was markedly impaired. The visual fields were full to rough tests. The pupils were equal, regular in outline and reacted poorly to light and to accommodation. Turning of the eyes to the left was slightly defective. There was marked horizontal nystagmus on looking to either side, which was coarser to the right. The nystagmus was rotary on looking upward. Impairment of sensation on the left side of the face was noted, and both corneal reflexes were diminished. Bilateral nerve deafness was present; it was more marked on the left side. The gait was very ataxic.

Course.—A diagnosis of bilateral tumor of the auditory nerve was made and a suboccipital craniotomy was carried out by Dr. Scrimger. However, the patient's condition would not allow incision of the dura, so that the cerebellum was not exposed. Following the operation the patient rapidly became blind and the hearing much worse; she grew gradually weaker, so that further operation was not deemed advisable.

Paralysis of the intercostal muscles and disturbance of sensation of pain below the cervical segments, suggesting compression of the spinal cord, were observed by Dr. Cone on the day before death. The patient died on Oct. 3, 1928, of respiratory paralysis. Clinically, the multiplicity of the tumors stamped this case as von Recklinghausen's disease.

Gross Pathology.—A necropsy was performed fourteen hours after death. Our gratitude is due Professor Horst Oertel for permission to make the following study. The body was that of a normally developed woman, 153 cm. in length.

Peripheral Tumors: Many multiple subcutaneous nodules were noted over the surface of the body, one measuring 3.5 by 2 cm., situated over the right deltoid muscle, and another, 2 cm. in diameter, below the right nipple. On section these nodules were seen to be encapsulated, pale gray, lobulated and firm. On opening the abdomen a small, pale gray, well encapsulated tumor, 1 cm. in diameter, was seen in the mesentery of the ileum. Another small nodule 2 by 1 cm., of the same consistency, was present along the lesser curvature of the wall of the stomach, about 6 cm. from the pyloric ring. It did not involve the mucosa of the stomach. A nodular thickening of the nerve as it entered the right suprarenal gland was present. The suprarenals were firm, pale yellow and rather granular; they were normal in size and shape.

Sympathetic Nervous System: The sympathetic ganglia were enlarged by numerous irregular thickenings, which on section appeared firm and nodular. The largest of these formed an oval tumor, 3.5 cm. long, which displaced the right suprarenal gland forward. This tumor was definitely attached to the sympathetic ganglion on that side.

Cranial Nerves: On removal of the brain a large, firm and encapsulated tumor attached to the left auditory nerve was seen, measuring 5.5 by 3.5 cm. It compressed and distorted the pons, medulla and cerebellum (fig. 1 *A*). On section, it was observed to have the consistency of a raw potato. It had irregular areas of fibrous tissue and contained smaller areas of old hemorrhages. A large blood-vessel was seen to course through the tumor. The corresponding internal auditory meatus was widened to measure 1.5 by 0.8 cm.

A smaller tumor, the size of a split pea and well encapsulated, was seen in the right cerebellopontile angle arising from the right auditory nerve about 1 cm. from

its exit (fig. 1 *B*). The right facial nerve was attached to this tumor. A small tumor was attached to the left oculomotor nerve just after its exit from the midbrain; it lay below the left posterior cerebral artery (fig. 1 *C*). A smaller tumor in the substance of the right trigeminal nerve was present just after the nerve made its exit from the pons (fig. 1 *D*). The left trigeminal nerve had an irregular nodular thickening immediately beyond the gasserian ganglion. Pinhead-sized tumors were seen along the glossopharyngeal, the vagus, the spinal accessory and the hypoglossal nerves (fig. 1 *E*). Thus, all the cranial nerves were involved with the exception of the first, second and fourth.

Spinal Nerve Roots: Throughout the entire length of the cord the dorsal ganglia appeared relatively large (fig. 2 *C*). Attached to the sixth right cervical

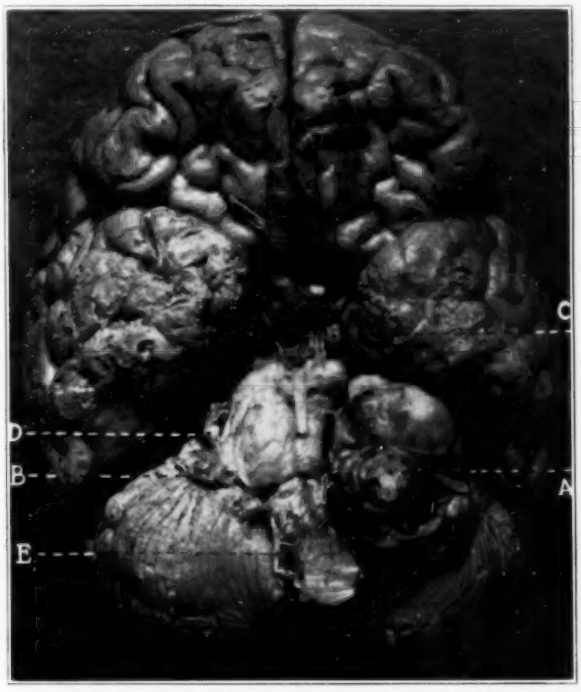

Fig. 1.—Base of the brain. *A* indicates a tumor of the left auditory nerve; *B*, a tumor of the right auditory nerve; *C*, a tumor of the left oculomotor nerve; *D*, a tumor of the right trigeminal nerve, and *E*, tumors of the glossopharyngeal and vagus nerves.

root was a firm, pale gray tumor, measuring 3.5 cm. by 1.5 cm., about the center of which there was a definite constriction where the tumor and nerve went through the intervertebral foramen forming a dumbbell-shaped tumor. The tumors were rare on the anterior roots, except in the region of the cauda equina where they became numerous on all the roots (fig. 3). Here and there in the course of the nerve roots were larger swellings measuring about 5 mm. in diameter. Along the course of one nerve root of the cauda equina fifteen small nodules were counted.

Dura Mater: In the falx cerebri there were a number of small yellowish-white nodules which were firm and grayish white in appearance on cross section.

Irregular areas of yellowish-brown, loosely adherent material were attached to the inner surface of the dura around the spinal cord. Scattered throughout the entire length of the inner surface there were many small nodules measuring about 4 by 4 mm. They appeared to be budding off from the under surface of the dura and projecting a distance of about 2 or 3 mm. These tumors were attached to both dorsal and ventral portions of the dura without bearing any relation to the

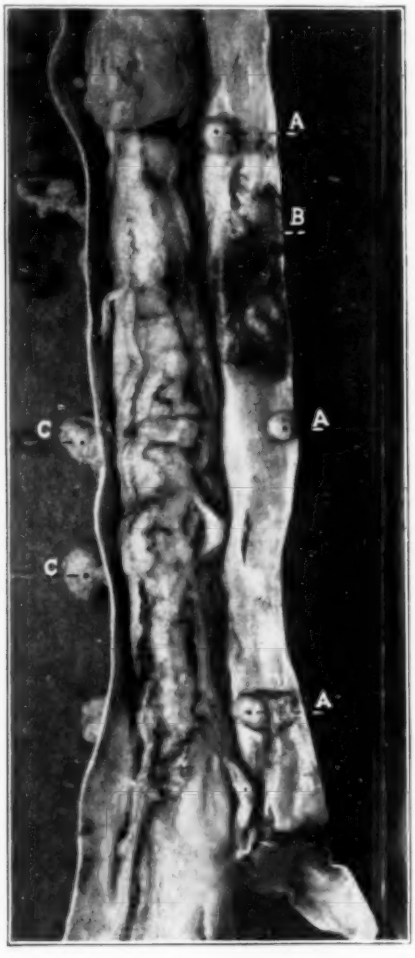

Fig. 2.—Dorsal spinal cord with membrane attached. *A* indicates a meningeal fibroblastoma of the dura; *B*, wartlike elevations on the dura, and *C*, enlarged dorsal root ganglia.

nerve roots (fig. 2*A*). The dura was attached to the arachnoid by filamentous adhesions to an unusual degree. Further, several areas of a warty character were scattered over the under surface of the dura (fig. 2*B*). These measured about 5 mm. in diameter. They presented a flat, pebbly appearance and did not appear to be encapsulated.

Brain: The convolutions of the brain were flattened and somewhat pale. The ventricles were markedly dilated. Small, soft scattered areas were seen in the brain, chiefly at the junction of the gray and white matter. These softened areas were rough to the touch, and some appeared to have small cavities in them. The anterior poles of the thalami presented similar areas. The splenium of the corpus

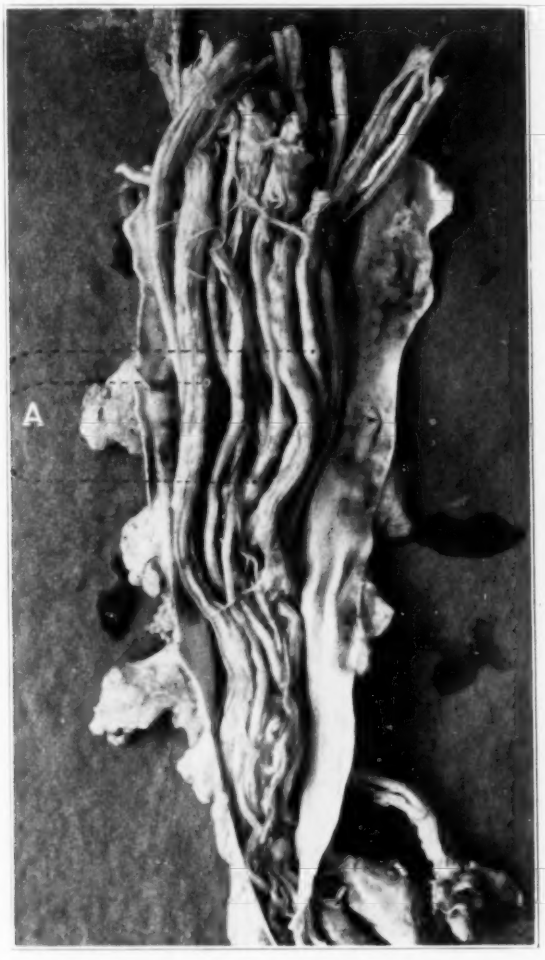

Fig. 3.—Multiple tumors of the cauda equina.

callosum contained a definitely softened area. A small cyst was seen at the junction of the gray and the white matter in the parietal lobe.

Spinal Cord: The spinal cord presented an odd appearance. Portions were ballooned to a diameter of 2.5 by 1.5 cm. and definitely demarcated by constriction above and below. The whole cord was wrinkled, wavy and irregular in outline and shape (fig. 2). Cross section of the cervical region of the cord showed a long, grayish-white tumor, intramedullary, measuring 1.5 by 1 cm. This was easily distinguishable from the surrounding cord substance. Other areas of the

cord on cross section were edematous and swollen. Many small, grayish-white tumor areas, situated either centrally or peripherally, were scattered throughout the substance of the spinal cord. Some of these tumors contained small cysts, and in one a small fresh hemorrhage was evident.

Cases of von Recklinghausen's disease with neoplastic alteration in the nerves, meninges and central nervous system, although rare, are on record. Generalizations of surprisingly divergent nature have resulted. The study of such a case should cast new light on the nature of the biologic process which is responsible for the condition.

Fig. 4.—Nerve fibers passing through the connective tissue hyperplasia of the dorsal root; Gross-Bielschowsky method.

Microscopic Pathology.—Spinal Nerve Roots: As noted in the gross description, there were numerous nodular enlargements of the spinal roots and of nearly all the cranial nerve roots, varying from a growth the size of a millet seed to the large acoustic tumor and the "dumbbell tumor" in the cervical region.

The histologic structure of these tumors was, in general, uniform. They presented the characteristic tangled intermixtures of connective tissue, nerve fibers and sheath of Schwann cells. The nerve fibers wandered through this tangle, often alone and without any definite pattern (fig. 4). The caliber of these fibers varied greatly. They sometimes presented large fusiform swellings or balls in their course. The myelin sheaths likewise showed zones of abrupt enlargement to a greater extent than normal.

In addition to this reticular structure there were areas in some of these tumors which resembled perineural fibroblastoma (solitary neurofibroma of Thompson). The elongated nuclei were arranged in bundles or currents (fig. 5) and palisading was frequent (nuclear rows of Verocay). Streaming between these nuclei were numerous long slender fibers of unvarying caliber which swept through the tissue (fig. 6). These fibers (hair fibers) were stained selectively by reticulin stains (Hortega, Foote, Laidlaw or Perdrau methods). With a van Gieson stain they assumed a yellowish-brown tone. With Mallory's phosphotungstic acid stain these reticulin fibers stained red or yellow, and fibroglia fibers were demonstrable

Fig. 5.—Cell pattern resembling the perineural fibroblastoma of the dorsal root; hematoxylin and eosin.

in blue, a further evidence that the type cell in these neoplastic areas was the fibroblast.

Nerve fibers were much more rare in such areas of the tumor than in the tangled areas, but they were also found as single fibers, often nonmyelinated. There were occasional small areas of degeneration.

In the course of the nerve roots, even where grossly normal, small patches of overgrowth of connective tissue were found frequently, which resembled the tangled areas of the nerve tumors. In such areas the penetrating nerve fibers were spread out (fig. 7).

Comment.—Virchow long ago denominated these tumors as false neuromas, recognizing that a true neuroma must contain multiplying nerve cells, and it was early recognized that the striking characteristic of the affected nerves in neurofibromatosis was an overgrowth of the connective tissue lining the nerve (Wood in 1829, Smith in 1849, von Recklinghausen in 1882). However, both in the solitary nerve tumors and in the von Recklinghausen tumors the presence of tissue with palisading nuclei and parallel fibers led Verocay [18] to assume that the neoplastic cells were sheath of Schwann cells and that the fibers were

Fig. 6.—Collagen fibers (reticulin and hair fibers) in the perineural fibroblastoma of the dorsal root; Laidlaw connective tissue stain.

nerve fibers. He therefore proposed calling them all neurinoma, meaning nerve fiber tumor, a name which unfortunately has been widely accepted.

Without pursuing the discussion further from an historical point of view, the name perineural fibroblastoma was proposed by Mallory,[19]

18. Verocay, J.: Multiple Geschwülste als Systemerkrankung am nervösen Apparate, Festschrift f. Chiare, Vienna, 1908, p. 378.

19. Mallory, F.: The Type Cell of the So-Called Dural Endothelioma, J. M. Research, **4**:349 (March) 1920.

as he recognized the type cell of these tumors to be the fibroblast. Penfield [20] suggested that the formation of these long hairlike fibers was a characteristic of the connective tissue cells about the neurilemma sheaths and he showed that the fibers could be selectively stained with silver (Hortega connective tissue method). He further showed that in the tumors of von Recklinghausen's malady nerve fibers were to be found passing through the tumor substance, whereas in the solitary nerve tumors, which occur most frequently on the acoustic nerve or

Fig. 7.—Nerve fibers penetrating the nodule of the cauda equina; Gross-Bielschowsky method.

dorsal spinal roots, nerve fibers are found only passing around the tumor and not through it.

It therefore becomes logical to retain the time-honored term neurofibroma for von Recklinghausen's disease. These tumors are invariably made up of tissue of tangled or reticular structure (Antoni, type B

20. Penfield, W.: The Encapsulated Tumors of the Nervous System, Surg. Gynec. Obst. **45**:178, 1927.

tissue) and sometimes contain areas of true perineural fibroblastoma (Antoni, type A). The tangled areas are evidence of a connective tissue reaction to that obscure abnormality which seems to be characteristic of nerve fibers in this disease. Whether there is deficient insulation of the nerve fiber on the part of the sheath of Schwann, as has often been suggested, or whether there is some other cause for the stimulus is a matter for speculation. Abnormal nerve fibers (fig. 4) may be seen to wander through such areas of connective tissue, as already indicated,

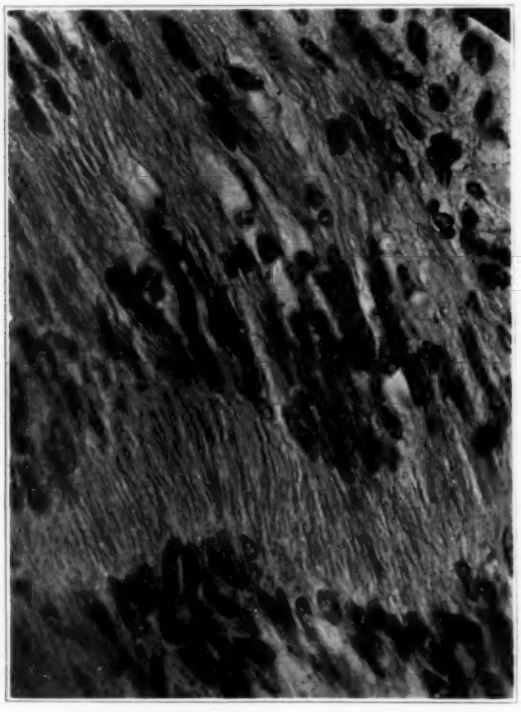

Fig. 8.—Palisading of the nuclei in a perineural fibroblastoma of the acoustic nerve; phosphotungstic acid stain.

but the observed alteration in these nerve fibers may be the result rather than the cause of the cellular reaction.

In numerous neurofibromas which we observed in other cases there was no formation of fibroblastoma areas. The appearance of these new growths within the neurofibroma is an additional phenomenon, no doubt also the outcome of local irritation of some sort.

Thus the background of the neurofibroma is a malformation (Misbildung) and the superimposed fibroblastoma a new growth (Neubildung), which is analagous to the gliosis and glioma formation within the central nervous system, which will be described.

Peripheral Nerves: On the whole, tumors on the peripheral nerves were less numerous in this case than those on the roots. The microscopic pattern was similar to that of the tumors of the roots, with exception of an even larger proportional amount of fibroblastomatous tissue.

Cranial Nerves: The tumors on these nerves were typical neurofibromas in which there were many areas of neoplastic fibroblastic growth, just as in the

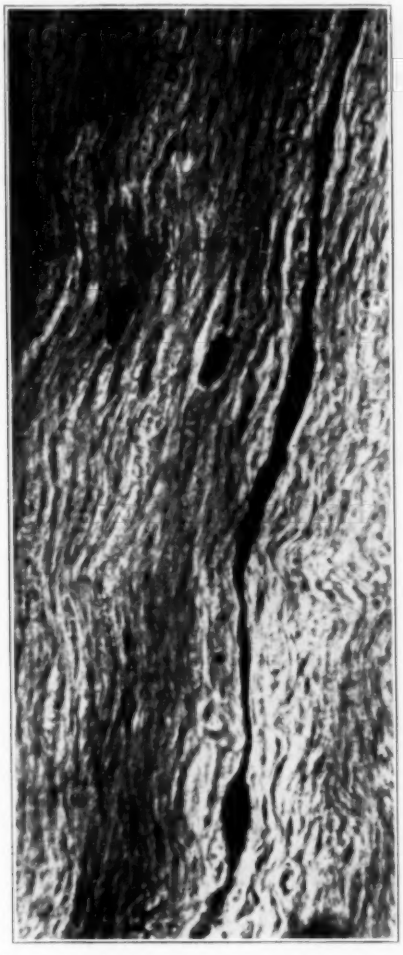

Fig. 9.—Nerve fibers wandering through a perineural fibroblastoma of the acoustic nerve; Gross-Bielschowsky method.

tumors of the spinal roots. The superimposed fibroblastoma occasionally was so large as to leave only small areas of typical neurofibroma tissue, and the penetrating nerve fibers were reduced in number to an occasional wandering thread. In the acoustic tumor was found marked palisading of nuclei (fig. 8). By the Gross-Bielschowsky method (fig. 9) and by myelin sheath stains, fine nerve fibers were shown to pass through the tumor. The neurilemma cells on these nerves, as

shown by Morgan's stain, were easily distinguished from the fibroblastoma cells by their greater slenderness. The included nerves were particularly scarce in the areas of fibroblastoma.

One trigeminal nerve tumor contained a typical perineural fibroblastoma with palisading of the nuclei. In the third cranial nerve were three or four small cell groups around vessels. When stained with phosphotungstic acid these cells were seen to have formed fine blue-staining fibers. They resembled to a certain extent the astrocytomas of the central nervous system. These patches were different

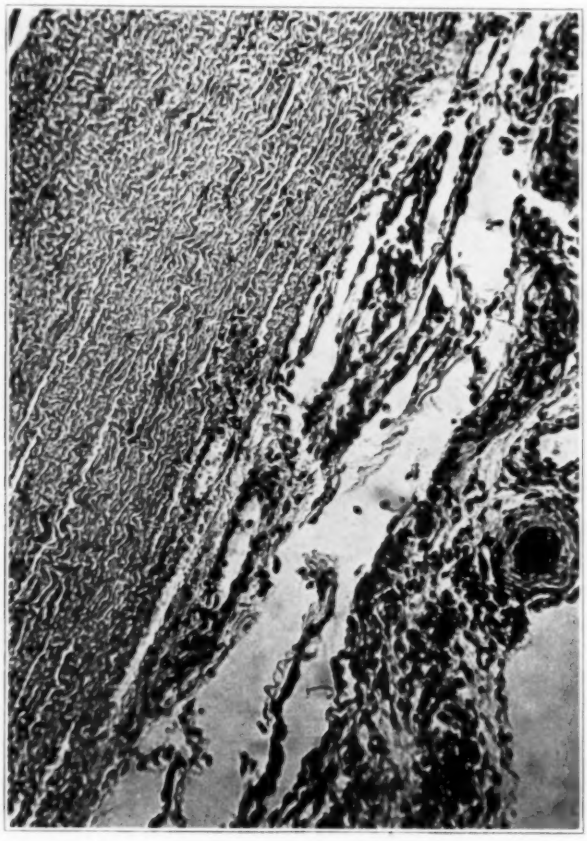

Fig. 10.—A wartlike elevation on the under surface of the dura; phosphotungstic acid stain.

from the cell groups already described but were too small to permit a considered opinion as to whether or not the cells were neurilemmal.

No changes were seen in the optic nerves.

Meninges: The low discolored wartlike elevations on the under surface of the spinal dura contained groups of arachnoidal cells which resembled those of the arachnoid tuft (fig. 10). The structure could hardly be considered typical of a dural tumor. These cell clusters were considered to be in the stage of reaction and possibly a forerunner of neoplastic growth.

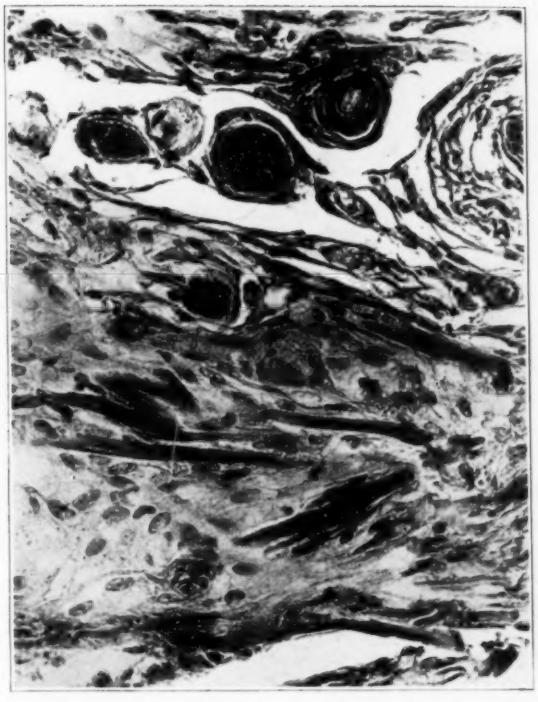

Fig. 11.—A meningeal fibroblastoma of the falx; hematoxylin and eosin.

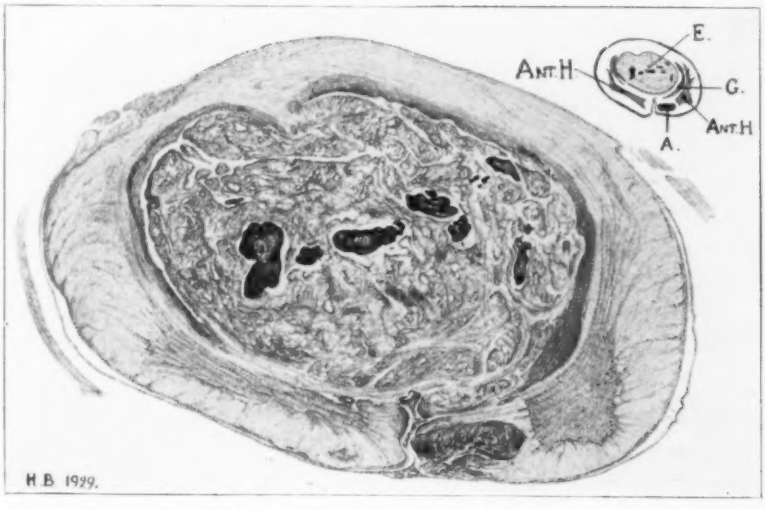

Fig. 12.—A drawing of a cross section of the spinal cord. *Ant. H.* indicates the gray matter of the cord; *E*, ependymoma; *G*, surrounding gliosis, and *A*, astrocytoma; phosphotungstic acid stain.

The larger nodules were likewise on the inner surface of the dura. A diagnosis of meningeal fibroblastoma (dural endothelioma, psammoma, meningioma) was made. The type cell contained a proportionally large nucleus with plentiful cytoplasm. The cells formed small whorls and there were numerous psammoma bodies (fig. 11). There were a moderate number of giant cells and some cells with multiple nuclei. Within some of these cells an opaque colloid substance was seen, apparently the forerunner of the psammoma bodies. The collagen of these tumors, in contrast with the slender fibers of even caliber seen in the neuro-

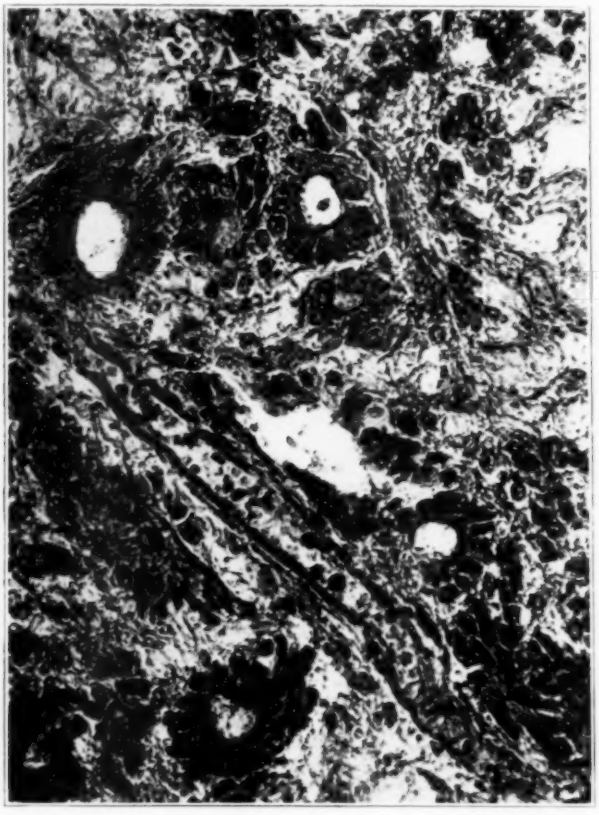

Fig. 13.—An ependymoma of the spinal cord; phosphotungstic acid stain.

fibromas, was made up of irregular ribbon-shaped strands with little tendency to parallelism.

However, it must be noted that there were departures from the usual picture of meningeal fibroblastoma. The cells in some areas showed more tendency than usual to regiment and sheaf formation as in the perineural tumors. Such tumors contained few whorls and the collagen was made up of slender fibers the arrangement of which somewhat recalled a perineural fibroblastoma. However, neither nerve fibers nor myelin sheaths could be stained in any of these meningeal tumors.

In cross sections of the spinal cord an arachnoid tumor was discovered which was so small as to have escaped gross examination. This tumor was not attached

to the dura, was growing in the meshes of pia-arachnoid and was histologically a meningeal fibroblastoma.

Comment.—The meninges showed a tendency to neoplastic growth, producing tumors that are made up of fibroblasts with characteristics peculiar to the cells of the meninges. In addition to this neoplastic

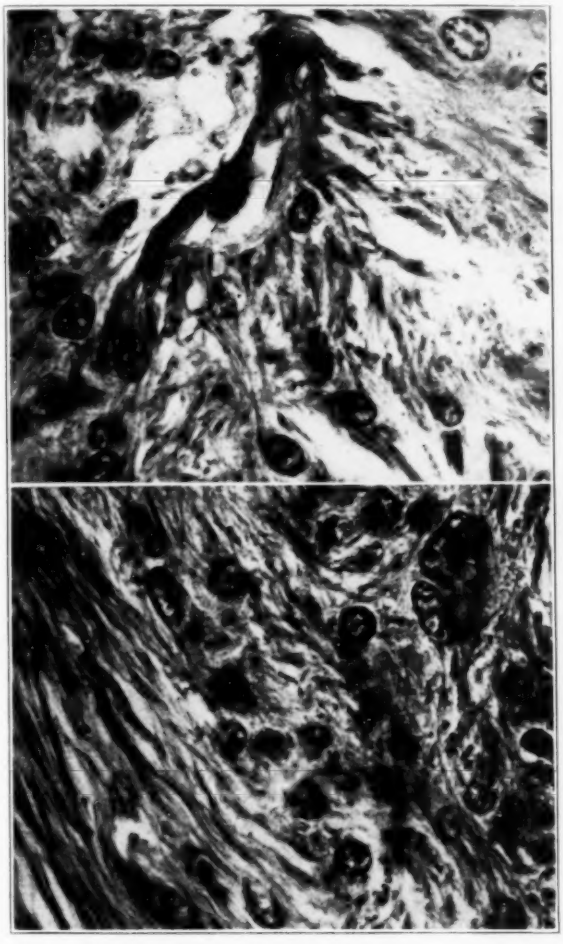

Fig. 14.—An astrocytoma of the spinal cord; phosphotungstic acid stain.

growth there was evidence of non-neoplastic reaction of the same cells in the warty eruptions of the dura.

Some of these neoplasms appeared on the under surface of the dura with little or no attachment to the arachnoid, and some within the meshes of the pia-arachnoid. This indicated that these tumors may grow from tufts of the arachnoid as originally suggested by M.

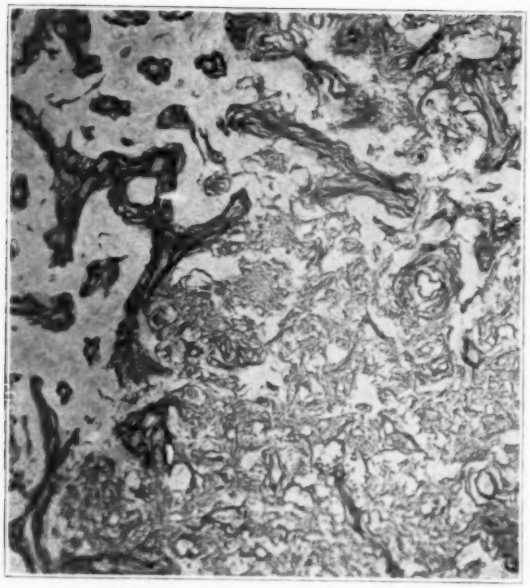

Fig. 15.—A patch of overgrowth of the bloodvessels in the cerebrum; Laidlaw connective tissue stain.

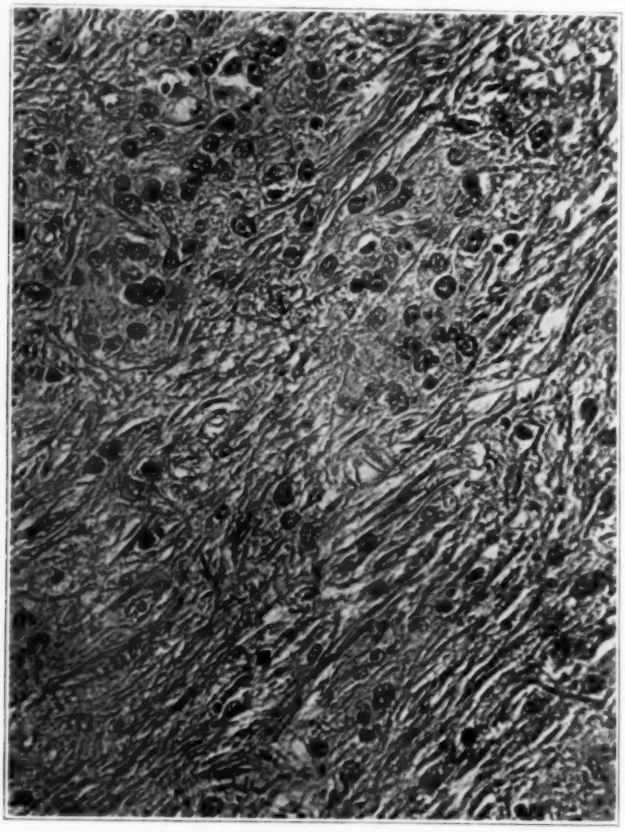

Fig. 16.—An astrocytoma of the cerebrum; phosphotungstic acid stain.

Schmidt,[21] but that analogous cells may also give rise to them on the under surface of the dura. Meningeal fibroblastoma would seem, therefore, to be a somewhat better term than arachnoidal fibroblastoma.

Spinal Cord: In one section there was a large, centrally placed tumor. Owing to the size of the tumor the cord here was about twice the normal diameter. This tumor was a typical ependymoma (fig. 12 *E*). There were many small ependymal rings, and large strips of typical ependyma formation (fig. 13). In places, cilia were to be seen. Some of the cells which were not part of the ependymal rings seemed to have laid down neuroglia fibers. The tumor was moderately vascular; no mitotic figures were seen. Specific nerve fiber stains showed only an occasional nerve fiber in the tumor; these were practically all near the periphery. Myelin

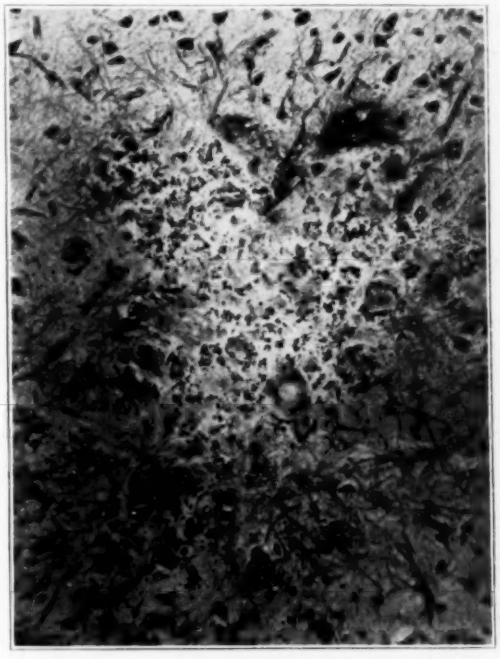

Fig. 17.—A patch of glial reaction in the cerebrum with a granular deposit at the center; Cajal's gold chloride sublimate.

sheath stains also showed that the occasional myelinated nerve fiber was near the periphery of the tumor. Around the tumor was a zone of neuroglia astrocytes (fig. 12 *G*) which resembled the cells of an astrocytoma.

A most surprising observation in the same section that showed the ependymoma described, was the presence of a discrete nodule of tissue near the ventral surface of the cord, but embedded in its substance (fig. 12 *A*). This nodule was moderately cellular; the nuclei, for the most part, showed a rather loose formation of chromatin. There were but a few giant cells. The cytoplasm was largely filled

21. Schmidt, M.: Ueber die Pacchionischen Granulationen und ihr Verhältnis zur den Sarkomen und Psammomen der dura mater, Arch. f. path. Anat. **170:** 429, 1903.

with numerous, fine, long fibers which were stained blue with Mallory's phosphotungstic acid stain (fig. 14); these fibers were often parallel but sometimes tangled. Many of these fibers ended perpendicularly about the small vessels, demonstrating their nature to be neuroglial. The nodule must be considered a rather cellular astrocytoma.

At another level in the spinal cord there was a definite neuroglial reaction. There were many large glia cells with opaque, plentiful cytoplasm. At one point

Fig. 18.—Hyperplasia of cells resembling astroblasts about a small vessel of the cerebellum; phosphotungstic acid stain.

in this area there was a small collection of astrocytes which seemed to have taken on the aspect of the neoplastic astrocytes in an astrocytoma. There was likewise a small cyst in this area. In the same section, overlying the cord was an area of typical meningeal fibroblastoma growing in the pia-arachnoid as already described.

Cerebrum: In the cerebrum there was an area, near the surface of the cortex, of widespread change in the vessels (fig. 15). They were much increased in

number and much thickened, the thickening of the vessels sometimes obliterating them. In some areas the vessels were packed closely together so that there was almost no room for other tissue between. Neuroglial stains showed that the astrocytes were large and fibrous, though still present between the vessels. Nerve cells had largely but not entirely fallen out. Oligodendroglia was not stained here. The reaction was definitely vascular, and the section might justify the diagnosis of hemangioma.

There was another separate area in the cerebrum with a marked increase of astrocytes, which had the microscopic appearance of an astrocytoma (fig. 16). In part this was very cellular, and in another part the cells were widely separated and a small cyst had formed.

In addition to these two neoplasm-like areas of change there were small circumscribed patches of abnormal neuroglia; the astrocytes were large and contained bizarre-shaped, often multiple nuclei. In the center of these patches, as shown by gold chloride, there was a curious collection of granular pigment (fig. 17).

Cerebellum: In the cerebellum there were numerous areas of focal gliosis just beneath the pia. In one area there was a collection of astrocytes of such a character that one would do well to call it an astrocytoma. In another area of the cerebellum the blood vessels were surrounded by a collar of neuroglia cells which were typical of astroblasts (fig. 18). The areas were not close enough together to justify naming the area astroblastoma.

In addition, there were areas of gliosis scattered through the cerebellum, as in the cerebrum and spinal cord. The gliosis was a reaction of astrocytes. Oligodendroglia did not seem to take part in the process, but the gliosis wherever seen was focal and not diffuse.

GENERAL COMMENT

Multiple tumors have been described in three different tissues of the body: the connective tissue sheaths of nerves, the meninges and the central nervous system. In all, the nature of the tumor is peculiar to these same tissues under other circumstances. In addition to the neoplasms, however, there are to be found in each of the three tissues (nerve trunks, meninges and central nervous system) areas of hyperplasia of the same cells which in other areas have become neoplastic.

Nerve Trunks.—The tangled or reticular tissue which constitutes the background of all neurofibromas should be considered a connective tissue (and probably also a sheath of Schwann) reaction about the fibers of the nerve. The nerve fibers are not neoplastic. Thickening of the nerve trunks, which may be generalized in these cases, is caused by just such perineuronal hyperplasia of the connective tissue about nerve fibers. When the reaction is marked, a swelling is found on the nerve which must literally be called a tumor, but which in a strict sense cannot be called a neoplasm. Such pure neurofibromas are apt to undergo jelly-like hyaline degeneration.

Antoni pointed out clearly that this "reticular apolar tissue" was always present in neurofibromas; he called it type B. This tissue does not show palisading of nuclei or polarization of the cells. Tissue of

Antoni's type A, which is sometimes present, possesses both of these characteristics. It is truly neoplastic, the type cell being the fibroblast, peculiar to nerves, which normally forms long slender collagen fibers, thus giving strength to the nerve trunk and relieving nerve fibers from strain. This second type of tissue then, which is sometimes present, is superimposed perineural fibroblastoma (Penfield [22] 1927, 1928).

However, a solitary nerve or nerve root tumor, which is always a pure perineural fibroblastoma, can easily be distinguished from a neurofibroma containing areas of fibroblastoma, by the fact that the former has nerve fibers about its capsule but not passing through it. On the other hand, neurofibromas will be found to have some nerve fibers straying through the tumor tissue.

Meninges.—The flat wartlike pigmented patches on the under surface of the dura, as pointed out, are made up of hyperplasia of arachnoidal cells, such as are evidently the starting point for meningeal fibroblastoma (Schmidt). The presence of blood pigment-laden cells suggests some vascular disturbance also. Such a hyperplasia of the cells, which elsewhere on the under surface of the dura have become neoplastic, constitutes a reaction that is analagous to the reaction of connective tissue about the nerves. Both reactions may be considered, perhaps, preneoplastic.

Central Nervous System.—However, there is a further analogy to be found in the central nervous system when patches of gliosis are scattered through the brain and cord. These patches contain typical reacting astrocytes of adult and not embryonic character. There are patches of ependymal hyperplasia as well. These two types, ependymal cells and astrocytes, are highly differentiated products of the spongioblastic series, and they are the cells which have given rise to multiple tumors.

Further, the remarkable areas of hyperplasia of the blood vessels, which might almost be called hemangioma, have many forerunners in that there are patches of increase of vessels and thickening of vessel walls, which constitute hyperplasia of the same structure. However, with regard to the blood vessels it is more difficult to draw a line between hyperplasia and neoplasia.

So far as the changes of the central nervous system in von Recklinghausen's disease are concerned, Bielschowsky and Rose [23] (1927) were the first to point out that the cells involved were not embryonic. They disagreed with Antoni on this point, although they acquiesced with the

22. Penfield, W.: Principles of the Pathology of Neurosurgery, Nelson's Loose-Leaf Surgery, New York, Thos. Nelson & Sons, 1927, chap. 6, p. 303.

23. Bielschowsky, M., and Rose, M.: Zur Kenntniss der zentralen Veränderungen bei Recklinghausenscher Krankheit, J. f. Psychol. u. Neurol. **35**:42, 1927.

contention of Verocay and Antoni that the peripheral tumors are neurinomas formed from Schwann cells. If the peripheral tumors were made up of Schwann cells instead of fibroblasts, the astrocytomas of the central nervous system could be likened to them.

The key to the identity of these tumors lies in the nature of the fibers elaborated. The neurofibromas form reticulin (or collagen) fibers which stain orange with Mallory's phosphotungstic acid stain. Further, they are demonstrated selectively with reticulin stains and, aside from staining specificity, they possess a form which makes the diagnosis of nerve fibers inconceivable, as there are no fusiform enlargements and no collaterals. Their form is likewise entirely unlike that of neuroglia fibers. The fibers of the central astrocytomas stain blue with Mallory's phosphotungstic acid (like neuroglia fibers elsewhere) and they may often be seen to end on a vessel or connective tissue septum in a way that is characteristic of neuroglia fibrils.

We therefore agree with Bielschowsky and Rose that the central changes are regressive ones beginning with adult cells. We point out, on the other hand, that the same is true in the peripheral nerves. There the reactionary and neoplastic process is carried out by fibroblasts which preserve their differentiated characteristics, and not by glial cells in any sense. We have pointed out already that the dural tumors likewise are not formed from rests but from differentiated fibroblasts.

Therefore throughout the three tissues in which neoplasms appear there is to be found definite evidence of hyperplastic reaction of the cells peculiar to those tissues. This indicates that in von Recklinghausen's disease an irritant or stimulating influence is exerted on various tissues, causing hyperplasia in them. Superimposed on or sequent to this effect is the appearance of neoplastic growth of these cells.

Recent work on the production of tumors (Oertel [24] and Ricker [25]) suggests that previous to neoplastic growth of cells there is a stage in which, owing to some neurovascular stimulus, the cells that are destined to become neoplastic undergo a hyperplastic change. It is also a well known principle that a chronic irritant is capable, under some conditions, of initiating tumor growth. The suggestion may be made that the congenital defect in the nervous system is in some way capable of producing the necessary irritation of adjacent tissues. This irritation produces hyperplasia of the cells which are susceptible to stimulus and, as a secondary process, widespread neoplastic change may then take place among these stimulated cells.

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24. Oertel, H.: A Broader Outlook on the Tumor and Cancer Problem, Can. M. A. J. **20**:288, 1929.

25. Ricker, G.: Pathologie als Naturwissenschaft, Berlin, Julius Springer, 1924, p. 261.

One striking fact about all the neoplasms described is that none of them is neurogenic; that is to say, in every case the type cell of the neoplasm itself is not nervous in origin. Moreover, in none of the tumors can the type cell be said to be embryologically undeveloped. The tumors reproduced by the fibroblasts of the two different types (meningeal and perineural) preserve the peculiar characteristics of the connective tissue in question, and the same may be said of the ependymomas and astrocytomas with their ependymal rings on the one hand and plentiful neuroglia fibers on the other.[26] This fact speaks in favor of the production of the tumor by means of an irritative process rather than from some embryologic rest.

What the original congenital defect may be is only conjecture. We find no difficulty in subscribing to the doctrine that that defect may lie in the sheath of Schwann, although there is as yet no proof of it histologically. The manifestations of the disease are plain for us to study and compare. The cause of all of these manifestations is part of the unsolved mystery of neoplastic growth which may fall to another generation to disclose.

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26. It is of interest that neoplastic astrocytes do not resemble the astrocytes of the normal brain in cell outline. Being packed together they are often elongated and often perivascular foot plates cannot be found, while in the central nervous system these vascular attachments are always present. One may be misled by a superficial histologic resemblance of the astrocytomas to the neurofibromas if proper stains are not used with discretion. Also some of the meningeal fibroblastomas have unusually fibrous areas which resemble neurofibroma superficially, if nothing but poorly made hematoxylin and eosin stains are relied on. It is the cytoplasmic differentiation which must be relied on—not simply the nuclear form.

MYASTHENIA GRAVIS WITH STATUS LYMPHATICUS AND MULTIPLE THYMIC GRANULOMAS *

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The pathology of myasthenia gravis is still the subject of a great deal of controversy. Pathologic material is difficult to obtain and when obtained studies of the pathology offer such a variety of results that a satisfactory explanation of this peculiar clinical picture has not been arrived at as yet. It is essential that all cases of myasthenia gravis with definite pathologic observations should be recorded, not only for the reason of their rarity but that they may serve toward the construction of an explanation of the pathology of this disease, confirm a part of it or offer useful hints for future observations.

The case reported in this paper offered a great deal of material for such considerations.

REPORT OF CASE

Clinical History.—Mrs. A. R., a white woman, married, aged 31, was admitted to the New York Post-Graduate Hospital on September 26 and died six hours after admission. She complained of dysphagia, dysphonia, general weakness, difficulty in breathing and loss of weight. The illness began about six months before admission with ptosis of both eyelids; she had had no trouble with vision. Four months after this, she could not laugh but could eat. One month later, she began to experience difficulty in speech. This gradually grew worse. For the last ten days before admission the patient could not swallow. She had no fever and no pain. Gradually, weakness developed in the muscles of the back of the neck and the jaw. Finally she had difficulty in breathing. In her past no history of acute infection could be traced. She had had no children and no miscarriages. Menstruation had been irregular, and she had menorrhagia.

Physical Examination.—The patient was undernourished and presented marked ptosis of both eyelids, more on the left than on the right side. There were an internal strabismus and bilateral paralysis of the face. The patient could not laugh or swallow and had considerable difficulty in speech and breathing. The muscle and tendon reflexes were normal. The blood pressure was 130 systolic, 80 diastolic. On spinal tap, 15 cc. of clear fluid was obtained which was entirely normal on detailed examination. The temperature was about 99 F.; the pulse

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* From the Department of the Laboratories, New York Post-Graduate Medical School and Hospital.

rate, 130, and the respiration rate, 28. The patient gradually became more dyspneic and cyanotic until death.

Postmortem Examination.—At autopsy the body showed emaciation. It measured 147 cm. in length. The long bones were thin. A hard nodule, the size of a walnut, was felt over the isthmus of the thyroid. Enlarged lymph nodes were palpable in both sides of neck, and also in the axillary and inguinal regions. The sternum had to be dissected from an adherent mass in the anterior mediastinum. This appeared to be an enlarged thymus gland which extended from the jugular fossa over more than half of the pericardial sac. The mass measured approximately 9 by 7 by 6 cm. It was well encapsulated. The capsule was covered with dense fibrous membranes and tags.

On section, a well defined nodule was seen occupying the center of the thymic mass (fig. 1). This nodule measured 6 by 4 by 4 cm. It had a thick fibrous capsule which was very hard and partly calcified, and which averaged from 5 to 8 mm. in thickness. The center of the nodule was pulpy, soft in consistency and purplish red. Fibrosis extended from the capsule irregularly through this parenchyma. A portion of this showed a rusty, reddish-brown hue; in other portions hemorrhages and yellow opaque areas were seen. The nodule was surrounded by fat intermingled with fibrous tissue. This fibrosis extended to the thyroid gland and backward over the arch of the aorta.

The thyroid gland was uniformly enlarged. The right lobe measured 70 by 38 by 28 mm., the left 60 by 33 by 23 mm. On section, the parenchyma presented a uniformly firm, meaty appearance. The colloid secretion was diminished throughout. There was obvious fibrosis. Embedded in the upper portion of the left lobe was a well circumscribed nodule measuring 12 mm. in diameter. It was well encapsulated, gray and firm. Immediately above the isthmus, at the junction with the right lobe of the thyroid, a nodule was found that was so hard that it had to be sawed through. On section it showed a thick fibrous capsule, in large part calcified. This nodule measured about 23 mm. in diameter. Its center showed the same purplish soft parenchyma seen in the thymic nodules. The capsule was irregular and almost entirely calcified; it measured from 8 to 13 mm. in thickness. The larynx was narrow and each of the vocal cords measured 14 mm. in length. The tonsils were uniformly enlarged and about 35 mm. in diameter. The muscles of the tongue, as well as those of the larynx and the deeper region of the neck, were slender and pale brown; they showed nothing striking. There were a great number of enlarged cervical lymph glands which measured from about 12 to 15 mm. in diameter. These were well encapsulated and on cross section showed reddish-brown soft tissue. The heart was small. It weighed 220 Gm. The wall of the left ventricle measured 8 mm. and that of the right 4 mm. in thickness. The arch and thoracic portion of the aorta measured 3.5 cm. in circumference uniformly. The wall of the aorta was thin, its surface smooth everywhere. The lungs contained air throughout; on cross-section, blood-stained, frothy fluid exuded. The mucosa of the bronchi was congested everywhere and covered with thick turbid mucus. The spleen weighed 160 Gm.; on section, the malpighian bodies were barely discernible; there was evidence of increased fibrosis; the pulp was rather firm. The suprarenal glands together weighed 9 Gm.; all of the layers were uniformly thin. The intestines showed nothing of note, except enlarged solitary follicles and Peyer's patches; the mucosa was smooth everywhere. The mesenteric and retroperitoneal lymph glands were enlarged, being from 10 to 20 mm. in diameter; they were well encapsulated and showed reddish-brown lymphoid tissue on section. The uterus was retroflexed and infantile; it had an elongated pear shape and measured 7 by 4 by 4 cm.; in the musculature a few

small fibromyomas were scattered, measuring from 5 to 12 mm. in diameter. The ovaries each measured about 4 cm. in diameter; scattered in the dense stroma were small cysts with a smooth lining and watery content. Both tubes were thin and firm. The brain and cord showed nothing unusual on gross inspection; the ventricles of the brain were narrow. The hypophysis measured 10 by 5 by 4 mm., and showed increased firmness.

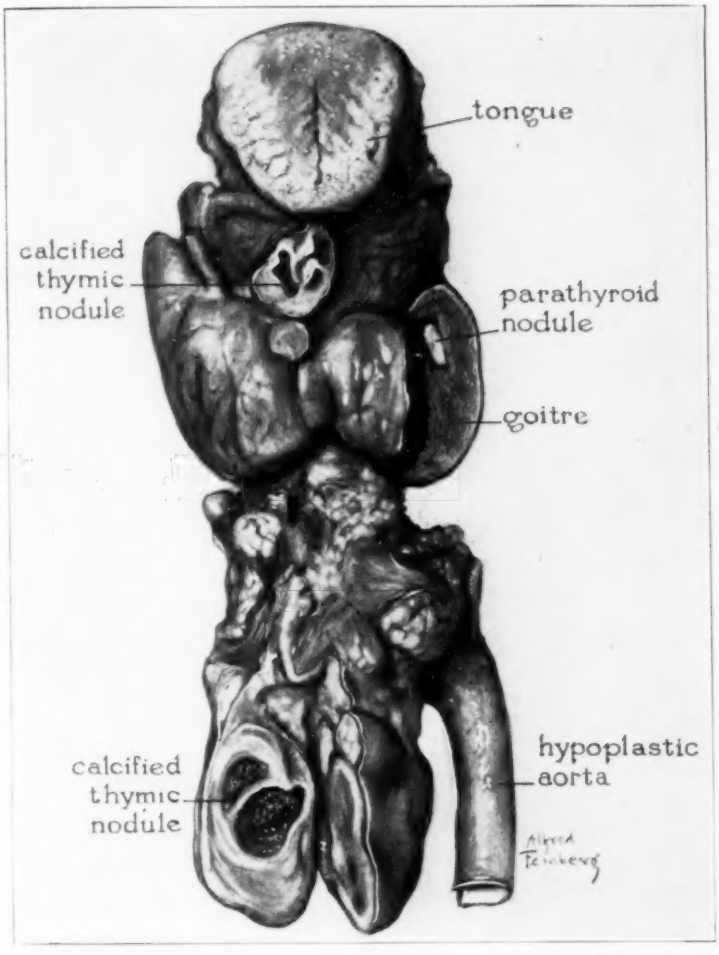

Fig. 1.—Organs of the neck, showing: mediastinal thymic granuloma; diffuse struma with accessory thymic granuloma above the isthmus and misplaced parathyroid in the left lobe, and hypoplastic aorta.

Histologic Studies.—On microscopic examination, the study of the mediastinal thymic nodule was of the greatest interest. The two usual cell types of the normal thymus were seen in the pulpy portion. There was, however, no trace of structural arrangement. In some fields the small round lymphoid cells, in others the large pale epithelial cells predominated (fig. 2). Both types, however,

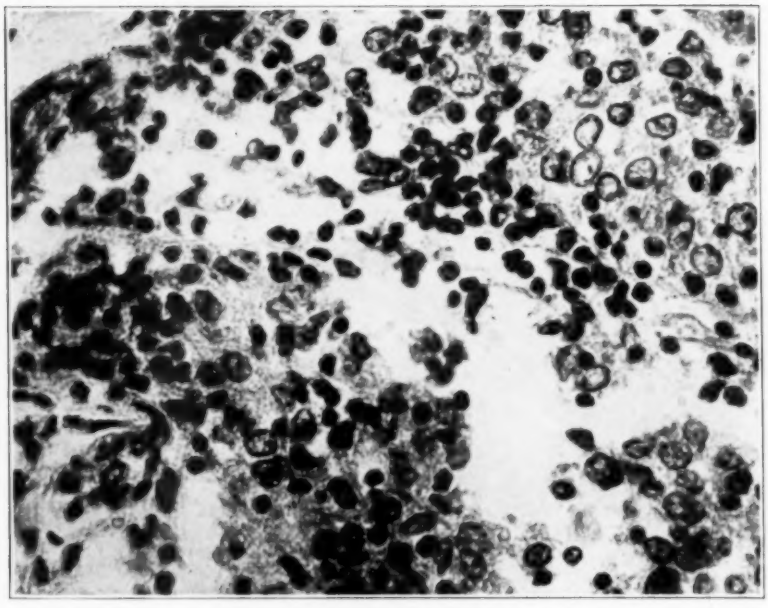

Fig. 2.—Mediastinal thymic nodule with loss of structural arrangement. The pale large epithelial cells and the dark small lymphoid cells are intermingled with inflammatory cells throughout.

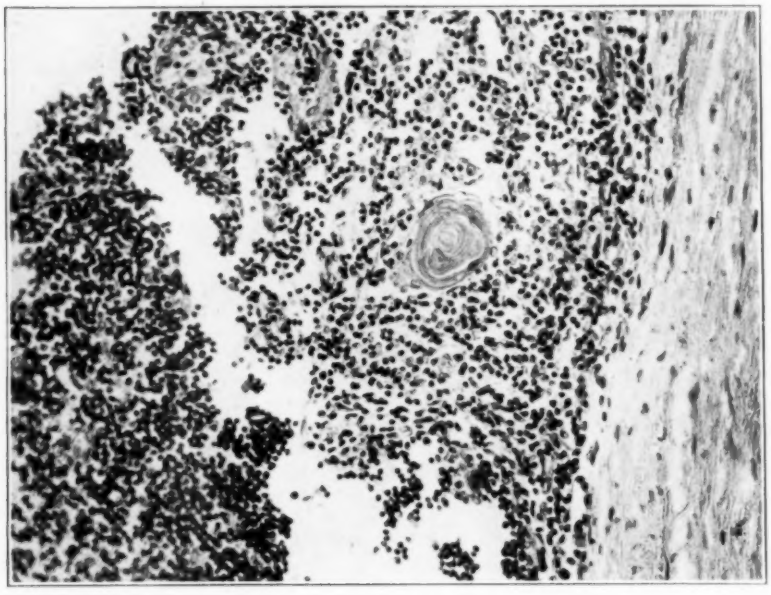

Fig. 3.—Periphery of a mediastinal thymic nodule, with thick fibrous capsule, and a large Hassal body.

were intermingled throughout and were separated into smaller and larger masses by fibrosis, most of which was old and partly hyalinized and contained numerous larger blood vessels. Young capillaries were numerous in the parenchyma, which contained a scanty polymorphonuclear infiltration throughout. There were also a few plasma cells and eosinophils here and there. The Hassal's bodies were rather few in number (fig. 3). They showed variety in size, but most of them were large. They were found rather near the capsule, surrounded for the most part by lymphocytes. An accumulation of epithelial cells was also seen, however, near the capsule. There was not even a suggestion of arrangement into cortex and medulla. The epithelial cells were polyhedral and had clear vesicular nuclei of uniform size. The outlines of their cytoplasm were vague. They had the

Fig. 4.—Portion of capsule with fused chromatin material and with fatty acid crystals surrounded by inflammatory granulation.

usual reticular arrangement. No mitotic figures were found. There were large areas of necrosis which were surrounded with old, partly hyalinized fibrosis containing irregular masses of fused chromatin substance, recent and old hemorrhage (fig. 4). There were numerous endothelial cells, many of which were filled with brown pigment. There were numerous lymph or blood vessels; none of them contained thrombi.

The nodule above the isthmus of the thyroid resembled the histologic picture of the thymic nodule in every respect. The Hassal's bodies were even more frequent than in the nodule of the thymus. A differentiation into cortex and medulla was also evident in many places (fig. 5). The medulla consisted of the usual epithelial reticulum with the interspersed lymphocytes and Hassal's corpuscles. Eosinophils and plasma cells were scattered everywhere. There were also necrotic

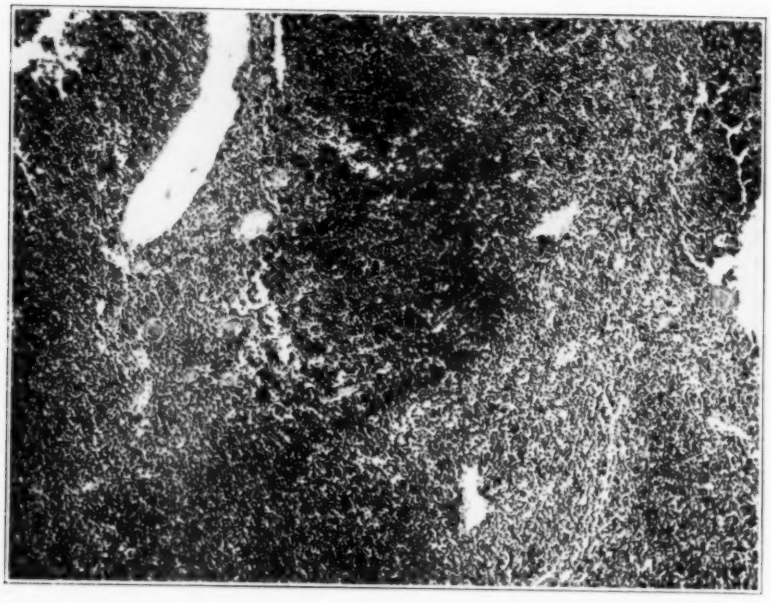

Fig. 5.—Accessory thymic nodule with differentiation of the cortex and medulla; numerous Hassal bodies are seen.

Fig. 6.—Necrotic portions of accessory thymic nodule with fatty crystals surrounded by foreign body granulation. Inflammatory cells of all types are scattered in irregular fibrosis.

areas that had a well defined fibrous wall which contained chromatin masses of destroyed nuclei and wandering cells of all types. Toward the necrotic areas, masses of fatty acid crystals were seen surrounded with typical foreign-body granulation tissue (fig. 6).

The thyroid gland showed unusual histologic changes. The interstitial tissue was increased throughout and contained infiltration, chiefly of lymphocytic type. There were a few polymorphonuclears also. The acini were lined by cuboidal epithelium which was hyperplastic in places. The lumina of many glands were narrow, with diminished thin secretion. The nodule in the left lobe of the thyroid consisted of interlacing strands and masses of polygonal epithelial cells such as are seen in the parathyroid (figs. 7 and 8). Some of these were elongated, had a pale-staining, rather clear protoplasm. A few oxyphil cells were also

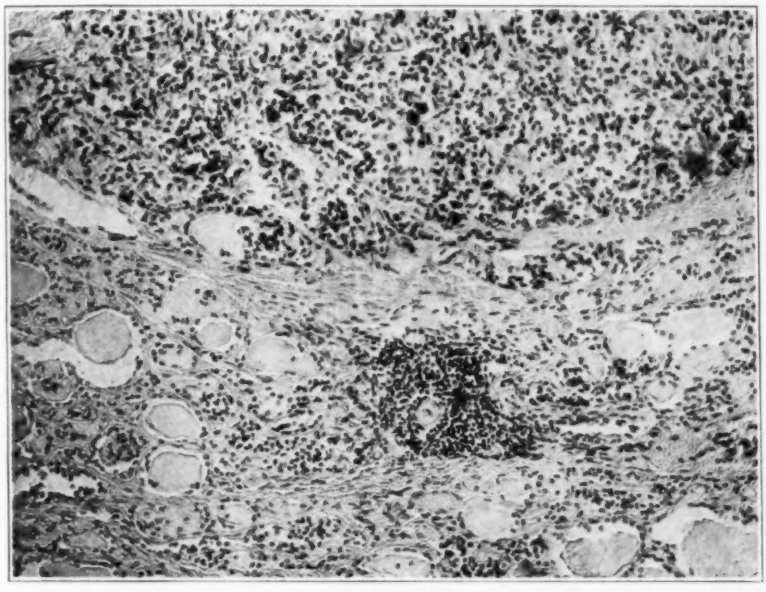

Fig. 7.—Border between the parathyroid nodule and the struma. Stroma of the goiter shows lymphoid infiltration; reduced from a magnification of × 60.

seen. There were a few tubular structures containing colloid secretion. The cervical lymph nodes showed in general the lymphoid structure, but a great deal of the parenchyma had been replaced by granulation tissue. The sinuses were wide and filled with wandering cells of all types; the eosinophil leukocytes were conspicuously numerous. The walls of the sinuses were lined by hyperplastic endothelial cells. The capsule showed increased fibrosis. The afferent vessels could be easily followed on account of their thick walls. In the center of the lymph node, dense fibrosis was seen.

Sections of striated muscle were taken from the masseter muscles, and the muscles of the tongue, pharynx, diaphragm and deep region of the neck (sternohyoideus). They all showed the same microscopic picture with slight variations (figs. 9, 10 and 11). There were large and small foci of lymphoid tissue, which were irregular in extension, surrounding the muscle fibers. Capillaries and larger

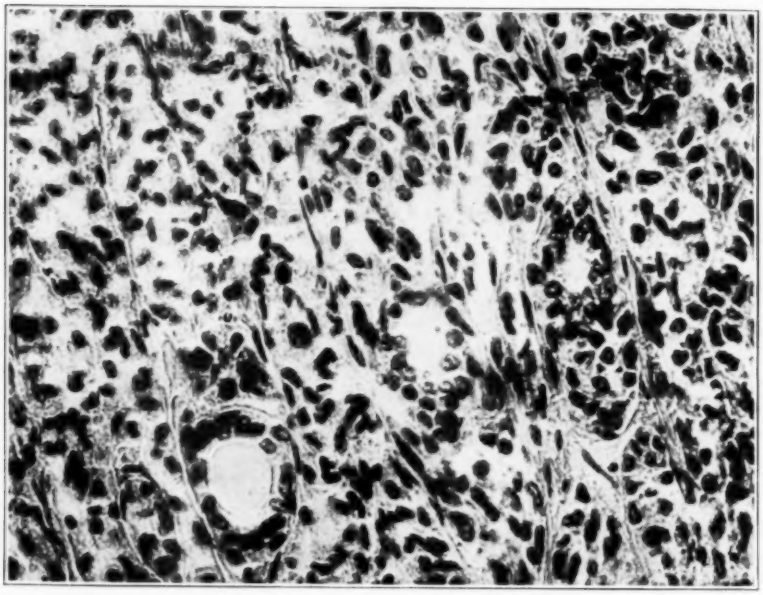

Fig. 8.—High power magnification of parathyroid nodule; reduced from a magnification of × 270.

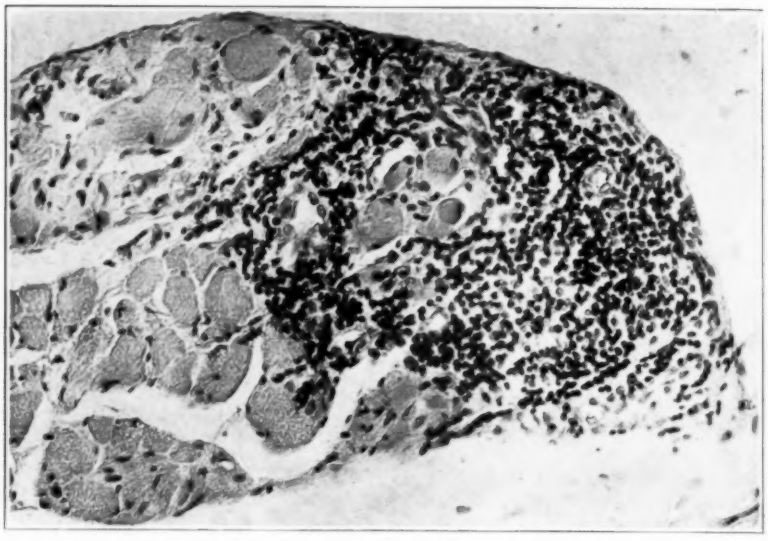

Fig. 9.—Hypoglossal muscle with lymphoid infiltration.

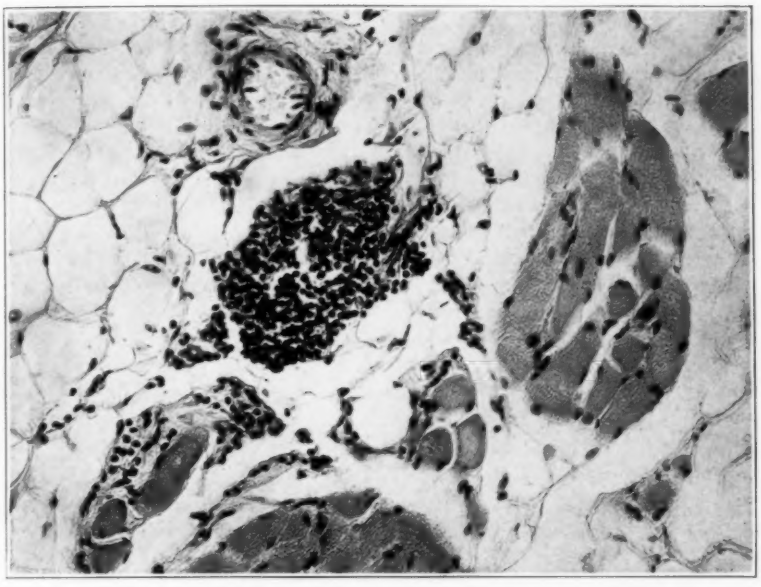

Fig. 10.—Masseter muscle with lymphoid tissue. The vessel is unchanged.

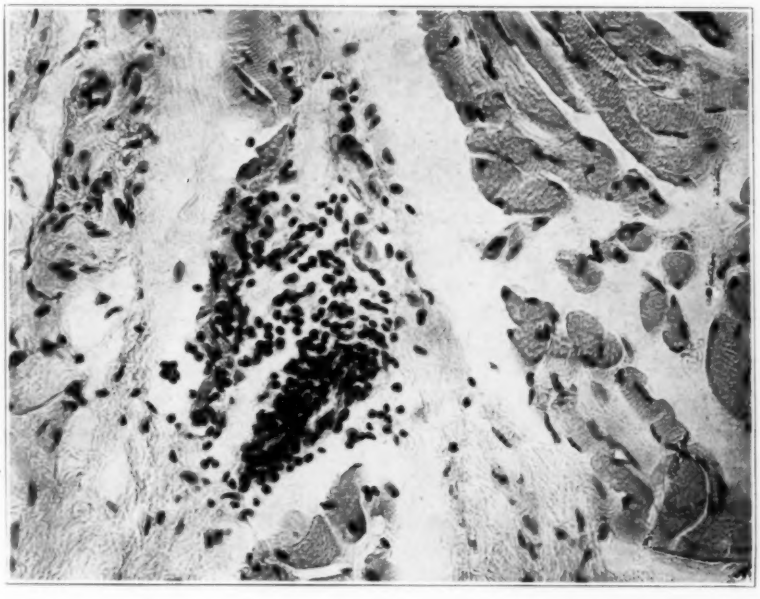

Fig. 11.—Diaphragm with lymphoid infiltration and atrophy of fibers.

arteries were seen crossing the foci or in the vicinity. The walls of these vessels showed uniformly well preserved structure. Among the various cell types the small dark round mature lymphocytes were the predominant cells. There were also a few plasma cells and polymorphonuclear leukocytes. In some of the foci the endothelial cells were more conspicuous than in others. Besides these lymphoid infiltrations, atrophy of the muscle fibers was also seen, not only in the areas adjacent to the lymphocytes but also in some fields free from such infiltration. These muscle fibers were much thinned out, showed vague striation and took the acid stains poorly, appearing almost clear.

Studies of the peripheral nerves revealed nothing of note.

Sections of the lung showed increased fibrosis around the bronchi with irregular foci of lymphocytes (fig. 12). Many of the bronchi were collapsed and filled with mucoid secretion.

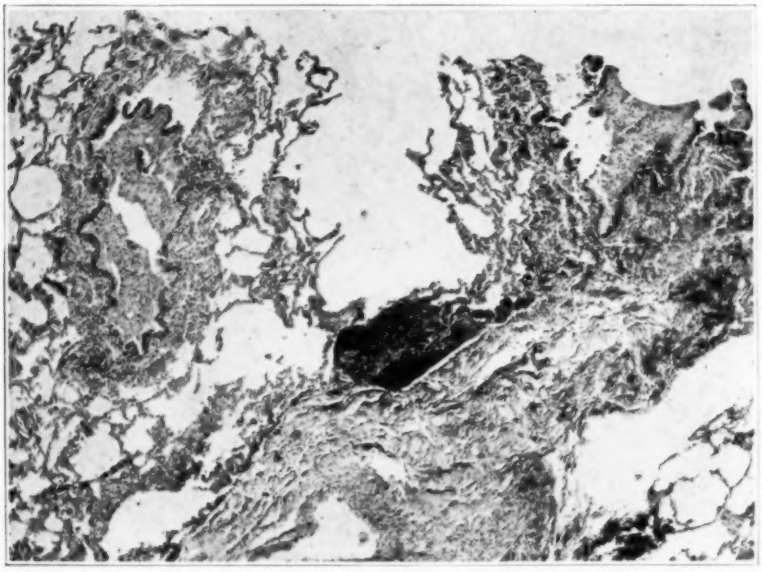

Fig. 12.—Bronchi of the lung filled with mucus; lymphoid infiltration.

Very few young follicles were found in the ovary. The stroma showed dense fibrosis with numerous blood vessels which had thick hyalinized walls. There were numerous cystic cavities lined by stratified, low follicular epithelium.

The chromaffin substance of the suprarenals was diminished. The medullary substance was atrophic (fig. 13).

The anterior lobe of the hypophysis consisted mostly of chief cells. The parenchyma was atrophic. The interstitial tissue showed old hyalinized fibrosis and a rich network of considerably dilated and congested capillaries (fig. 14).

Serial sections of the basal ganglia and of the base of the fourth ventricle of the brain showed no abnormal infiltration and no conspicuous changes. Some of the nerve cells showed a loss of Nissl bodies. Serial sections of the sylvian aqueduct showed nothing unusual.

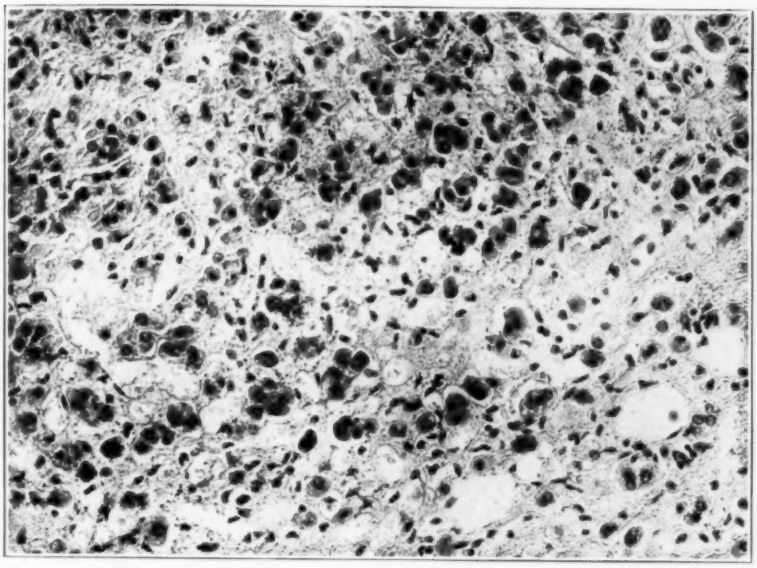

Fig. 13.—Atrophy of chromaffin cells of the suprarenals.

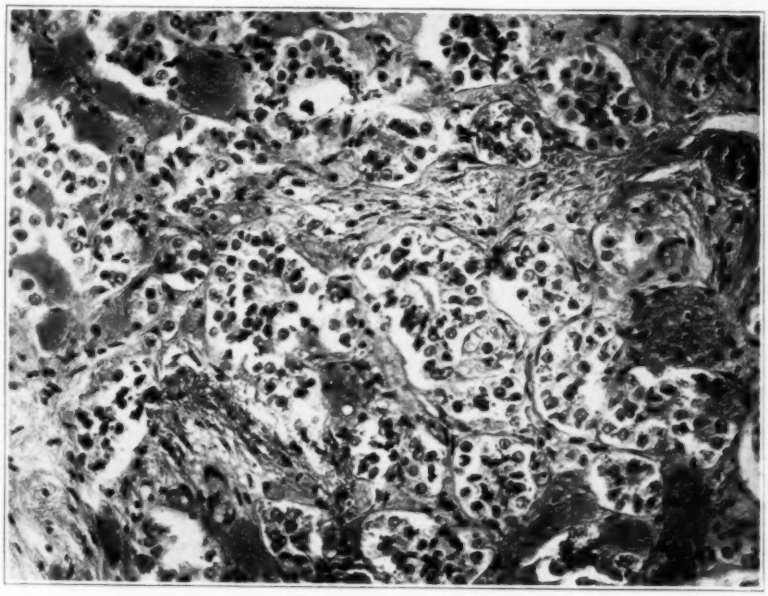

Fig. 14.—Fibrosis, congestion and atrophy of the hypophysis.

COMMENT

It may be of significance from the clinical standpoint, that this condition came about in a woman aged 31, without any other conspicuous previous illness. The only other feature recorded was the irregular function of the ovaries. The constitutional background has been often emphasized. Hart [1] reported this disease in two sisters. Curschman [2] found genital hypoplasia in the cases of two women. Bell [3] collected fifty-six cases with autopsy (1900-1917); seventeen of these showed enlargement of the thymus gland; ten others had tumors. Altogether, in almost half of these cases there was a thymic involvement.

The anatomic studies in the case recorded here disclosed the following conspicuous features:

1. There were two thymic nodules composed of the usual characteristic tissue elements. One was surrounded by involuted thymic tissue and fat over the pericardium. The other was abnormally placed over the isthmus of the thyroid. The normally situated thymic nodule showed a lack of structural arrangement which was mainly due to inflammatory changes. All the features of an active and chronic inflammatory process were present, with the resulting involutional fibrosis and the formation of a thick fibrous capsule. There was no evidence of any neoplastic condition. The histology of the thymic nodule above the isthmus of thyroid was structurally more normal than that of the nodule over the pericardium. Otherwise, both of these thymic nodules were composed of the normal constituents: lymphocytes, epithelial cell reticulum, Hassal bodies and eosinophils. Bell [3] made an exhaustive study of the thymic nodules in cases of myasthenia gravis and considered them of a neoplastic nature, although they showed essentially the same morphologic features as in the case reported in this paper. Bell gave no further report of the observations at autopsy. Hart [4] interpreted the histologic features as the result of repeated attempts at regenerative hyperplasia.

According to Grosser,[5] the main body of the thymus gland develops from the third pharyngeal pouch with the lower and outer parathyroid gland. An accessory thymus gland and the inner, upper parathyroid gland are derived from the fourth pharyngeal pouch. The origin of the

1. Hart, H. H.: Myasthenia Gravis with Ophthalmoplegia and Constitutional Anomalies in Sisters, Arch. Neurol. & Psychiat. **18**:439 (Sept.) 1927.

2. Curschman, H.: München. med. Wchnschr. **71**:1135, 1924.

3. Bell, E. T.: Tumors of Thymus in Myasthenia Gravis, J. Nerv. & Ment. Dis. **45**:130, 1917.

4. Hart, Carl: Thymus Befunde bei Myasthenia gravis pseudoparalytica, Virchows Arch. f. path. Anat. **220**:185, 1915.

5. Grosser, O.: Manual of Human Embrology, Keibel and Mall, Philadelphia, J. B. Lippincott Company, 1912, vol. 2, p. 461.

double thymic nodules and the misplaced parathyroid body can be readily understood, therefore, from the embryonic standpoint.

Both of the thymic nodules showed advanced inflammatory lesions with regressive changes. These were less marked in the accessory thymic nodule than in the one over the pericardium. The latter was probably first affected.

From the viewpoint of primary focus, it is of interest to note that Schumacher and Roth [6] reported marked improvement of myasthenia gravis after thymectomy. The lymphocytes present in their case returned to a normal count after the operation but the exophthalmic goiter which was also associated with the condition was not influenced. A great deal of evidence has been accumulated in favor of the view that status lymphaticus increases the susceptibility to infections (Symmers [7]). Bang's chemical studies are also of great interest. According to Bang,[8] the thymic tissue yields five times as much nucleic acid as other lymphoid tissues. Symmers accepted the liberation of nucleoproteins as an explanation of the cause of death in status lymphaticus.

SUMMARY

1. In the case reported in this paper the mediastinal thymic nodule shows the older inflammatory process with a great deal of destruction. Hart [9] collected a great deal of evidence in favor of a "thymogenic autointoxication" in cases of status lymphaticus. Whether the so-called lymphotoxicosis, which Schmincke [10] also spoke of, is of prime importance in the pathogenesis of myasthenia gravis, particularly in connection with inflammatory changes, remains a matter for further investigation.

2. A large parathyroid body in the left lobe of the thyroid gland gave added evidence in favor of multiple misplacement of the branchial structures. Bergstrand [11] pointed out the relationship between a large thymus and enlargement of the parathyroids. This was obvious in this misplaced nodule.

3. The relationship of parenchymatous goiter to enlargement of the thymus—first emphasized by Markham [12] 1885—is shown in 79 per

6. Schumacher and Roth: Thymectomie bei einen Fall von Morbus basedowi mit Myasthenie, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **25**:746, 1913.

7. Symmers, D.: Status Lymphaticus, Am. J. Dis. Child. **14**:463 (Dec.) 1917.

8. Bang, I.: Beitr. z. chem. Phys. u. Path. **5**:317, 1904.

9. Hart, Carl: Die Bedeutung der Thymus für Entstehung und Verlauf des Morbus basedowi, Arch. f. klin. Chir. **104**:347, 1914.

10. Schmincke, A.: Pathologic des Thymus, in Henke and Lubarsch: Handbuch der speziellen pathologischen Anatomie und Histologie, Berlin, Julius Springer, 1926, vol. 8, p. 799.

11. Bergstrand, H.: Acta path. et microbiol. Scandinav. **5**:52, 1928.

12. Markham: Tr. Path. Soc., London, 1885, vol. 9.

cent of cases by Capelle.[13] In addition, in our case chronic inflammatory changes were present in the thymus as well as in the thyroid gland.

4. The changes of the lymph nodes are also evidence of a long-continued active inflammatory process. The rich eosinophilic infiltration of the lymph nodes suggests some relationship to the condition found in the thymus. Badertscher[14] disproved Ehrlich's theory that the bone-marrow is the only source of these cells and brought evidence in favor of his view that, besides lymphocytes, the thymus also produces eosinophils.

5. The lymphocytic infiltration of the skeletal muscle has attracted a great deal of attention since Weigert's report in 1901. Weigert,[15] however, regarded the thymic nodule as a neoplastic growth and consequently the lymphoid tissue of the muscles as metastases. In 1905, Buzzard[16] did not accept the neoplastic nature of these tissues. Those in the muscle Buzzard considered to be lymphorrhages without any obvious relation to the thymus. Besides the lymphoid infiltration, Knoblauch found also extensive atrophy of the striated muscles. Marie, Bouttier and Bertrand[17] agreed with Buzzard that "lymphorrhage" is an appropriate name, although they found no changes of the lymph or blood vessels in the adjecent tissues. They declared that these lesions are of "obscure significance." Foxe,[18] in a clinical study, demonstrated the extensive atonia of the somatic as well as of the visceral muscles. Recently, Querido[19] made an extensive study of striated muscles, particularly the masseter, the tongue and the diaphragm muscles. As the walls of vessels running through such foci are infiltrated with inflammatory cells, Querido offered the hypothesis that myasthenia gravis is a general vascular disease, pathologically a vasculitis chronica proliferans. These lymphoid infiltrations of the muscles can be well correlated with the other observations in this case. Hyperplasia of the lymph system was found extensively in this case. At the same time,

13. Capelle: Ueber die Beziehungen der Thymus zum Morbus basedowi, Beitr. z. klin. Chir. **59**:353, 1908.

14. Badertscher, J. A.: Eosinophilic Leucocytes in the Thymus of Postnatal Pigs, Anat. Record **18**:23, 1920.

15. Laquer, L., and Weigert, C.: Beiträge zur Lehre von der Erbschen Krankheit, Neurol. Centralbl. **20**:594, 1901.

16. Buzzard, E. F.: The Clinical History and Post-Mortem Examinations of Five Cases of Myasthenia Gravis, Brain **28**:438, 1905.

17. Marie, H.; Bouttier, H., and Bertrand, I.: Étude anatomo-clinique d'un cas grave de myasthénie de Erb-Goldflam, Ann. de méd. **10**:173, 1921.

18. Foxe, A. N.: Report of a Case of Myasthenia Gravis with Visceral Symptoms and a Clinical Contrast with a Case of Dystonia Musculorum Deformans, J. Nerv. & Ment. Dis. **68**:134, 1928.

19. Querido, A.: On Myasthenia Gravis, J. Nerv. & Ment. Dis. **69**:522, 1929.

evidence of inflammatory changes was present in all the lymphoid tissue: thymic nodules, tonsils, lymph nodes, etc. The inflammatory features of the foci in the muscles are similar to those found elsewhere. Blood vessels are present in all these places but they are obviously not of primary importance. Their presence and their morphology are a part of the inflammatory change.

6. The other enlargements of lymph nodes and the hyperplasia of the intestinal lymphoid structures are a part of status lymphaticus. The other striking features of this condition are: the small heart, hypoplasia of the aorta, infantile genitalia with hypoplastic ovaries, hypoplasia of the chromaffin substance of the suprarenals, and atrophy of the hypophysis with fibrosis. Marie, Bouttier and Bertrand mentioned, in the autopsy report of their case, that the heart of the well developed, middle-aged woman weighed 200 Gm., but they laid no emphasis on it, and in other cases it is impossible to follow the general constitutional changes with accuracy from the records. Marie, Bouttier and Bertrand, as well as other French authors, particularly Sézary and Landouzy,[20] emphasized insufficiency of the suprarenal and pituitary glands in myasthenia gravis. This was present in the case reported in this paper and can be regarded as one of the features of status lymphaticus. Sézary therefore advocated suprarenal therapy. Later he combined this with extract of the pituitary body.

7. The morphologic studies of the brain and nervous system have given essentially negative results, except for some vague degenerative changes of the nuclei at the base of the fourth ventricle. Studies of the nervous system, both gross and microscopic, reveal no definite lesions. Oppenheim[21] reported in one of his cases an anomaly of the sylvian aqueduct which was divided into narrow channels.

Marine[22] emphasized the important fact, concerning status lymphaticus, that the thymus is not the chief and not the only organ involved in this condition. This is the main reason why the name status thymicolymphaticus had to be given up in favor of the term proposed by Paltauf[23] in 1889. Although, in myasthenia gravis, thymic enlargement with or without tumor nodules has been found in a large percentage of cases, careful study of the constitutional changes of all organs should be made in every case. Thymic enlargements can be readily diagnosed by means of roentgenology; such a case of myasthenia

20. Sézary, H.: Sur la pathogénie de la myasthénie, Bull. et mém. Soc. méd. d. hôp. de Paris **49**:724, 1925. Landouzy and Sézary: Myasthénie d'Erb et insuffisance surrenale, Soc. de neurol., May, 1912.

21. Oppenheim-Bruce, H.: Textbook of Nervous Diseases, London, T. N. Foulis, 1911, p. 1035.

22. Marine, D.: Status Lymphaticus, Arch. Path. **5**:661 (April) 1928.

23. Paltauf: Wien. klin. Wchnschr. **2**:871, 1889.

gravis was reported clinically by Beretvas.[24] Medical treatment so far has been without uniform success. Surgical measures, successfully employed in the case reported by Schumacher and Roth, require further investigations. These are important not only from a practical standpoint but also as regards the pathogenesis of myasthenia gravis. The peripheral histologic changes may account for a great many of the symptoms. Whether the lymphoid tissue in the skeletal muscle is of autochthonous or of blood stream origin is a question still to be answered. Studies of status lymphaticus are still indefinite in regard to this. As in the present case of an old inflammatory focus in the mediastinal thymic nodule, the possibility of blood stream distribution of the lymphoid tissue has to be considered. The secondary inflammatory changes may be due to the same agent that is responsible for the inflammatory granulomas. Such a granuloma is usually single. In the present case there were two present. There is strong evidence that the primary nodule is often present in the mediastinum; early removal of it may be of beneficial effect by preventing absorption.

The material presented in this paper not only furnishes certain positive information but also brings out many points that require further investigation.

CONCLUSIONS

1. Myasthenia gravis was associated with status lymphaticus in the case reported.

2. Multiple abnormalities of branchiogenic organs were present. A striking feature was the parenchymatous goiter with displacement and enlargement of parathyroid and thymic tissue.

3. The multiple thymic nodules were the site of extensive inflammatory changes. The mediastinal nodule showed evidence of a process of longer duration than the accessory nodule.

4. Study of the central and peripheral nervous system revealed nothing of significance.

5. The striated muscles showed extensive lymphoid infiltration and atrophy of the fibers.

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24. Beretvas, L.: Un caso di malattio di Erb-Goldflam con tumore de mediastino, Riforma med. **41**:771, 1925.

ALLERGY AS CAUSE OF EPILEPTIFORM CONVULSIONS *

GEORGE L. WALDBOTT, M.D.
DETROIT

Epileptiform convulsions occur as manifestations of various disorders, such as brain injury, infectious diseases in infants and uremia. Epilepsy that cannot be attributed to any known source is termed essential or idiopathic.

CLINICAL EVIDENCE

Attention has recently been focused on the theory that some obscure epileptiform convulsions may be due to hypersensitiveness. Research along this line has been undertaken by allergists as well as by neurologists. The former have found that in addition to the respiratory tract many other parts of the body, such as the genito-urinary and gastro-intestinal systems, are capable of manifesting allergic symptoms (Rowe [1]). It was, therefore, logical for them to include the central nervous system in their investigation as another possible seat of allergic manifestations (Vaughan [2]). Neurologists detected that epilepsy is occasionally associated with allergic conditions, especially migraine, and that the family history of epileptic members frequently points to hypersensitiveness. Spangler [3] obtained a history of the presence of allergy among the ancestors of 88 of 100 consecutive patients with essential epilepsy.

Ward and Patterson [4] tested 1,000 epileptic patients for skin sensitization and found 37 per cent sensitive to various proteins, whereas a control group of 100 normal persons gave only 4 per cent positive skin tests. A study undertaken by Wallis, Nicol and Craig [5] revealed that of 122 patients with epileptic convulsions 46 reacted positively to skin tests. Peptone, cereal, fish, meat, vegetable, eggs and milk were

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* Read at a meeting of the Detroit Neurological Society, June, 1929.

1. Rowe, A. H.: Food Allergy, J. A. M. A. **91**:1623 (Nov. 24) 1928.

2. Vaughan, W. T.: Allergic Migraine, J. A. M. A. **88**:1383 (April 30) 1927.

3. Spangler, R. H.: Allergy and Epilepsy: Analysis of One Hundred Cases, J. Lab. & Clin. Med. **13**:41 (Oct.) 1927.

4. Ward, J. F., and Patterson, H. A.: Protein Sensitization in Epilepsy, Arch. Neurol. & Psychiat. **17**:427 (April) 1927.

5. Wallis, R. L.; Nicol, W. D., and Craig, M.: The Importance of Protein Hypersensitivity in Diagnosis and Treatment of a Special Group of Epileptics, Lancet **1**:741, 1923.

the substances to which positive reactions were observed. Miller [6] and Howell,[7] who were among the early proponents of the allergic explanation of certain types of epileptic convulsions, pointed out the clinical similarity of asthma and epilepsy, emphasizing the hereditary factor, the onset of attacks following infectious diseases and the response of both asthma and epilepsy to foreign protein treatment.

Storm Van Leeuwen and Zeydner [8] detected certain substances that stimulate smooth muscle tissue in the blood of patients with epilepsy, urticaria, asthma and migraine. Since they failed to find this substance in normal persons they concluded that there may be some etiologic connection between these diseases.

EXPERIMENTAL EVIDENCE

It is generally known that in guinea-pigs a marked irritability of the central nervous system with violent convulsions often occurs during the course of the anaphylactic experiment. However, constant experimental production of epilepsy by this method has never been achieved (Claude and Montassut [9]). It is said that transfusion of blood from an epileptic to a normal person has given rise to convulsions (Spangler), and that in animals convulsions can be produced by the injection of blood from human beings who suffer from epilepsy (Antheaume and Trepsat [10]).

REPORT OF CASES

While it is not uncommon to note that asthmatic attacks are sometimes replaced by or associated with hay-fever, urticaria, angioneurotic edema and other allergic conditions, there are thus far no cases on record in which epileptiform seizures have substituted themselves for asthmatic attacks.

Two such cases are herewith presented.

CASE 1.—V. C., a boy, aged 2, was seen on June 8, 1926, on account of shortness of breath and wheezing. The mother and one sister had had epileptic seizures, and the patient had had eczema for some time. Asthmatic attacks started shortly after birth, and occurred at intervals of from four to five weeks.

6. Miller, J. L.: Epilepsy in Sensitization Disease, Am. J. M. Sc. **168**:635, 1924.

7. Howell, L. P.: Epilepsy and Protein Sensitization, Ohio State M. J. **19**:660, 1923.

8. Van Leeuwen, W. S., and Zeydner: Occurrence of a Toxic Substance in Blood of Cases of Bronchial Asthma, Urticaria, Epilepsy and Migraine, Brit. J. Exper. Path. **3**:282 (Dec.) 1922.

9. Claude, H., and Montassut, M.: Rôle of Anaphylactic Shock, Encéphale **22**:533 (July) 1927.

10. Antheaume, A., and Trepsat, L.: Pathogenesis of Epileptic Seizures, Encéphale **17**:103 (Feb.) 1922.

They were usually ushered in by vasomotor rhinitis. The examination revealed definite evidence of asthma. No skin tests were made at that time, and a blood count showed no eosinophilia. Roentgen examination of the chest revealed the enlargement of the hilum gland that is usually seen in asthma. On June 14, the mother said that the child had had two attacks which, according to her description, were typical of epilepsy with clonic and tonic convulsions, complete unconsciousness and loss of sphincter control during the seizures. The neurologic department corroborated the diagnosis of epilepsy. On August 5, I saw the patient during another attack of epilepsy. On August 14, the patient had another attack of bronchial asthma, which was relieved by the administration of epinephrine. Skin tests then revealed sensitiveness to eggs, corn, pepper and herring. The patient was free from both epilepsy and asthma for about one year after these foods were eliminated from his diet. The positive allergic family history, the presence of eosinophils at the time of epileptic attacks and the therapeutic test of eliminating the exciting foods, which was followed by improvement, point to some etiologic relationship between asthma and the convulsions.

Case 2.—W. B., a boy, aged 4, gave a history of constant cough associated with wheezing and dyspnea which had come on subsequent to pertussis and was of one year's duration. The patient had had eczema, but there was no family history of allergy. The examination on May 10, 1928, was negative for any pathologic condition of the chest, but the history of a chronic cough suggested a chronic bronchitis for which eight respiratory injections of vaccine were administered. At the conclusion of this treatment, the patient developed typical epileptiform seizures. He has had five such attacks. They came on during damp weather. On October 16, he was seen during an acute attack of bronchial asthma with all the physical and clinical signs of this disease. The attack was controlled by the use of epinephrine. Skin tests gave negative results. The neurologic department confirmed the diagnosis of epilepsy.

The striking feature in this case is the fact that the child had an allergic bronchitis (Waldbott[11]) which was not recognized as such at the first visit. He was treated for an infectious bronchitis by injections of vaccine. The vaccine apparently sensitized the patient to such an extent that he developed at first epileptiform convulsions and then definite asthma. He has lately been free from both conditions.

COMMENT

The question arises as to whether or not the occurrence of asthma and convulsions in these cases is incidental. The literature quoted and the observation of two additional cases of a similar nature leads me to believe that the convulsions in these patients were caused by allergy. In one of these cases, that of a girl, aged 23, who had been under my care, the patient was definitely sensitive to quinine. This drug had always caused her to have severe urticaria associated with allergic bronchitis. On one occasion she took quinine in order to induce an abortion. An attack was brought on that was, by her description, typical of epilepsy, but no urticaria and no bronchitis resulted. The other patient was one with chronic asthmatic and secondary bronchiectasis whom I once saw at his home during a severe attack

11. Waldbott, G. L.: Allergic Bronchitis, J. Lab. & Clin. Med. **13**:943, 1928.

of epilepsy that lasted for about thirty minutes. No clinical studies were carried out in either case.

In considering the pathologic changes which may lead to this peculiar type of allergy, one might speculate on the possibility of changes similar to urticaria or angioneurotic edema in certain cortical or meningeal areas. Possibly vascular spasms, edema and infiltration with eosinophils might be found in analogy with other allergic conditions. Autopsy reports of such cases are not, as yet, recorded in the literature, a fact easily explained by the transitory character of these attacks.

Another point of interest is the explanation of the benefit that has been obtained in some cases of epilepsy by the use of a ketogenic diet. Its value may be explained on the basis of either the accidental elimination of the specific proteins to which some epileptic patients may be sensitized or to the production of an acidosis which may alter the physicochemical make-up of the allergic person. It was recently observed by Hirsch and Williams,[12] and Barber and Oriel,[13] that there is a slight alkalosis during the allergic state, and that administration of alkalis increases the symptoms of allergy (Walzer[14]). In epilepsy, also, an alkalosis of the blood has been observed (Bigwood[15]).

CONCLUSIONS

The foregoing observations warrant a further investigation into the question of allergic epileptiform convulsions. In all patients with epilepsy of unknown origin a thorough study from an allergic point of view should be undertaken, including an allergic history, eosinophil counts and skin tests. Great discrimination, however, is necessary in doing this work; for, in all likelihood, only a small percentage of the cases of "essential epilepsy" belongs to this group.

SUMMARY

The cases of two patients suffering from epileptiform convulsions that alternated with asthmatic attacks are reported. It is held that the epilepsy was due to hypersensitiveness.

1056 Maccabee Building.

12. Hirsch, E. F., and Williams, J. L.: Hydrogen-Ion Studies: Changes in the Reaction of the Blood During Anaphylactic Shock, J. Infect. Dis. **30**:259, 1922.

13. Barber, H. W., and Oriel, G. H.: A Clinical and Biochemical Study of Allergy, Lancet **2**:1009 (Nov.) 1928.

14. Walzer, M.: Studies in Absorption of Undigested Proteins in Human Beings, J. Immunol. **14**:143 (Sept.) 1927.

15. Bigwood, E. J.: The Disturbance of the Acid-Base Equilibrium of the Blood in Epilepsy, Compt. rend. Soc. de biol. **89**:839, 1923.

News and Comment

PROGRAM FOR FIRST INTERNATIONAL MENTAL HYGIENE CONGRESS

The First International Congress on Mental Hygiene will be held in Washington, D. C., Hotel Willard, May 5-10, 1930. President Hoover has accepted the honorary presidency of this congress, and delegates are expected from more than thirty countries. Topics of the program are now ready for publication, and are contained in the form of a Preliminary Announcement, which can be obtained from John R. Shillady, Administrative Secretary of the Congress, 370 Seventh Avenue, New York.

Following are some of the general topics: 1. Magnitude of the mental hygiene problem as a health problem. 2. Organization of community facilities for prevention, care and treatment. 3. Organization of the mental hospital and its rôle in community life. 4. Psychopathic hospitals and psychopathic wards in general hospitals. 5. Care and treatment of mental patients outside of institutions. 6. Organization of special types of clinical service, as in courts of justice, outpatient departments of hospitals, communities, grade and high schools, colleges and social welfare agencies. 7. Types of personnel required in mental hygiene work. 8. Methods of training different types of personnel. 9. Clinical and social research in the field of mental hygiene. 10. Teaching of mental hygiene and psychiatry in medical schools. 11. Mental hygiene in industry, personnel work and vocational guidance. 12. Psychiatric social work, its scope and functions. 13. Mental hygiene aspects of delinquency, dependency, and other types of social maladjustment. 14. Marital relationships. 15. Social aspects of mental deficiency. 16. Mental hygiene and education; grade school, high school, college. 17 Special problems of adolescence. 18. Problems presented by children of special type: (*a*) the child with superior intelligence; (*b*) the neurotic child; (*c*) the child with sensory and motor defects. 19. Methods and possibilities of the child guidance clinic. 20. Significance of parent-child and teacher-child relationships in character and in personality development. 21. Parent and teacher training. 22. Mental hygiene of religious, ethical and moral teaching. 23. Problems of the preschool period. 24. Significance of these problems for the future of the child as individual and as citizen. 25. Possibilities in the future of human relationships in the light of an increasing knowledge of those factors that help and hinder the emotional, physical and intellectual development of the individual.

Names of speakers will be announced in advance of the Congress.

The American Psychiatric Association and the American Association for the Study of the Feebleminded will hold their annual meetings in Washington at the same time as the First International Congress. It is the purpose to have a maximum of discussion and minimum of formal paper-reading. To this end, papers at the morning sessions, printed at length in advance of the meetings, will be limited to ten minutes in statement, and discussion will follow. Afternoons will be given over to meetings of committees, prepared discussions that are not on the regular program, and recreation and sight-seeing. General sessions, designed to appeal widely to laymen, will be held on several evenings.

Members of the Program Committee are: Dr. Williams, chairman; Dr. C. Macfie Campbell, Director, Boston Psychopathic Hospital and Professor of Psychiatry, Harvard University; Dr. William Healy, Director, Judge Baker Foundation; Dr. Lawson G. Lowrey, Director, Institute for Child Guidance, New York; Dr. Howard W. Potter, Assistant Director, Psychiatric Institute and Hospital, New York; Dr. Arthur H. Ruggles, Superintendent, Butler Hospital, Providence, R. I.

In addition, persons residing in twenty-eight different countries are represented on the advisory committee on program. Besides these, the following are serving on the same committee, representing fields related to mental hygiene: *Anthropology*, Franz Boaz, professor of anthropology, Columbia University; *Education*, V. T. Thayer, Educational Director, Ethical Culture Schools, New York; *Eugenics*, Charles B. Davenport, Director, Department of Genetics, Carnegie Institution of Washington, Cold Spring Harbor, Long Island; *Industrial Psychology*, Walter V. Bingham, Director, Personnel Research Federation, New York; *Nursing*, Effie J. Taylor, Professor of Nursing and Superintendent of Nurses, Yale University School of Nursing; *Philosophy*, M. C. Otto, Professor of Philosophy, University of Wisconsin; *Psychiatric Social Work*, Mildred C. Scoville, President, American Association of Psychiatric Social Workers; *Psychology*, Lewis M. Terman, Professor and executive head of Department of Psychology, Stanford University, California; *Religion*, A. Eustace Haydon, Associate Professor of Comparative Religion, University of Chicago; *Sociology*, Ernest Watson Burgess, Professor of Sociology, University of Chicago.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

The subject for the 1930 Meeting of the Association for Research in Nervous and Mental Disease is Manic-Depressive Psychosis.

AMERICAN NEUROLOGICAL ASSOCIATION

The annual meeting of the American Neurological Association will be held in Atlantic City, N. J., June 9, 10 and 11, 1930.

Abstracts from Current Literature

RESEARCHES ON THE MICROSCOPIC CHANGES AND THE SPINAL FLUID IN DEMENTIA PRAECOX. V. M. BUSCAINO, Riv. di patol. nerv. **34**:181, 1929.

Buscaino presents his fourth synthetic and critical review of progress in research on dementia praecox. The first under the several headings is the review of the encephalographic observations of Jacobi and Winkler. These authors almost invariably found some dilatation of the lateral ventricles, often with fairly large fluid spaces over the cortex. The atrophy was most marked in the frontal lobes, was more frequent in the paranoid types and was not referable to the age of the patients.

Turning to the researches on the cerebrospinal fluid, it is reported that Marchand occasionally found increase in the spinal fluid pressure in the early months of the disease. Walter has continued his studies on the permeability of the meninges by the bromide method, with fairly concordant results showing decreased permeability in cases of dementia praecox. These observations have been corroborated by Hauptmann, Kral, Malamud, et al., and by Guttmann. Opinion is divided concerning the protein. Marchand finds it sometimes increased in the early stages and Kafka finds this increase constant, whereas others find no increase. Globulin is sometimes increased according to most of the authors cited, particularly Kafka. The proportion of globulin to total protein is somewhat higher than normal, although less than in the inflammatory and degenerative conditions of the nervous system. Ratner found deviations in the colloidal gold curve in all of twelve cases, whereas Bowmann found negative results in all of twenty cases. With colloidal benzoin, the reactions gave negative results. Kaltenbach found six abnormal curves in thirty-three cases by the normomastic reaction. The paraffin reaction was reported as negative; Pandy's reaction was almost negative, likewise Weichbrodt's. Buscaino's silver nitrate reaction showed a black color in one and maroon in the other of two cases. The normal reaction is grayish or faintly reddish. The reaction with syrup of citric acid, as carried out by Pagès, Benoit, Pélissier and Jaulmes, was positive in five of thirteen cases of dementia praecox and negative in fifteen healthy persons. Vizioli, by the potassium bichromate test, found four positive results among nine patients. Kral found hemolysin in traces in two of twenty-five cases. The Wassermann reaction was positive only when syphilis coexisted. Pleocytosis, taking the normal as 1 cell per cubic millimeter, is noted in four of twenty cases by Bowmann and two of twenty-five by Kral. Spectrographically, Winkler found that after deproteinization of the fluid the absorptive power remained unchanged in traumatic cases, was slightly increased in six of twenty-four phrenasthenic cases and diminished in all the others. In schizophrenic patients the absorptive power was considerably increased in 80 per cent, more so in the later stages of the disease.

Turning now to microscopic studies, a number of authors have described thickening of the meninges with mild cellular infiltrations, which they think are important indications of morbid processes going on in the cranial cavity. Mild proliferation of the adventitia of the blood vessels has been reported a number of times, particularly by Marchand. Perivascular deposits of lipoid material are found frequently, together with irregularly distributed areas of hyperemia and anemia. Developmental anomalies in the brain have been scarce, Pfeiffer failing to find binucleate ganglion cells in a careful investigation of six cases. Atrophy of the ganglion cells with lipoid infiltration practically to the point of disintegration, vacuolar degeneration and chronic cell disease have been reported by most authors who have studied the brains in such cases. The most thorough work is probably that of Fünfgeld, based on eleven early cases. The reviewer considers his work most important and gives a fairly detailed account of it. Sclerotic alterations in the cells, with more or less abundant lipoid change, are more frequently encountered

in the later stages of the disease. In the early cases there is a filamentous transformation of the protoplasm, with disappearance of the Nissl bodies and scattering of dark granules, especially at the base of the cell. There are thinning of the nuclear membrane, condensation of its chromatin and a tendency for this to become confused with the surrounding protoplasmic mass. It appears that the cells are undergoing hydropic degeneration, and this condition was not found accentuated among twenty control cases. The localization is principally in the third and fifth layers. At the same time, in the sixth layer swollen cells and nuclei can be seen. The areas affected are chiefly frontal and supramarginal. The intracellular fibrils and neurofibrils sometimes appear swollen. Increase in the protoplasmic glia and glia nodules is reported by Münzer, and "infectious nodules" by others. Rarefaction of the intracortical and subcortical nerve fibers, with deposits of metachromatic granules, is described in other cases, with swelling of the axoplasm, vacuolization and accumulations of granules and other substances in the vacant spaces. In the basal ganglia, the alterations are less notable than in the cortex. In certain cases fat is found in phagocytic cells grouped about the vessels. Areas of grapelike disintegration are found in a considerable number of cases in both the thalamus and the striatum. The corpus luysi appears normal. The floor of the third ventricle shows pathologic alterations in certain cases. The mesencephalon and pons appear unchanged. In the cerebellum, Cajal describes a number of abnormal observations such as thin dendrites of the Purkinje cells with irregular swellings and ballooning of the terminals, abnormal arborization, disappearance of the cells and marked rarefaction of the pericellular network of fibers; in addition, there are fewer mossy fibers in the lamina granularis. Cajal writes: "The cerebellum shows unequivocal signs of degeneration and destruction of cells and fibers, but there are, in addition, conclusive signs of regeneration and repair of the dendrites." The medulla, spinal cord and ganglia seem fairly normal. In the sympathetic ganglia, however, according to Dide, there is infiltration of granules in the protoplasm and its prolongations, with considerable swelling in the early stages and atrophy in the later stages. The pericellular reticulum is broken up and then seems to disappear. The connective tissue of the capsule reacts. In the ependyma and choroid plexus, Fünfgeld frequently finds vacuolization of the epithelium, with some hyalinization, proliferation here and there, and, in one case, cystic degeneration. The subependymal neuroglia is thickened in certain places, according to Steck.

Thus, it would seem that dementia praecox is constantly, and from the beginning, accompanied by pathologic variations in the chemistry and structure of the nervous system. Moreover, the publications of the last few years seem to bring confirmation to the author's views that the extracortical centers participate in the process, particularly in catatonic cases; that the lesions are minute and irregularly scattered, and that the proportionate number of grapelike areas of disintegration is generally larger in dementia praecox than in control cases. These again point to histochemical alterations in the brains of schizophrenic persons. Buscaino devotes many pages to the discussion of the grapelike areas of disintegration, giving the views pro and con that have been expressed since he first described them and mentioned their significance. He does not say that they are characteristic of dementia praecox, but claims that they are indicative of serious degeneration in the brain.

FREEMAN, Washington, D. C.

THE TREATMENT OF EPILEPSY. EDITORIAL, J. A. M. A. **95**:1560 (Nov. 16) 1929.

The history of the changing methods in the treatment of epilepsy, particularly to prevent the characteristic seizures, would fill a large volume. Medicinal aids, as a recent writer (Zabriskie, E. G., in Cecil's Textbook of Medicine, Philadelphia, W. B. Saunders Company, 1927) has pointed out, have included drugs that are of benefit in the general hygiene of the patient, such as cathartics and tonics; those that are intended to combat certain specific diseases whose amelioration is

associated with improvement of the epileptic manifestations, as syphilis and malaria; and sedatives, whose purpose is to diminish the frequency and severity of the attacks or to arrest them. Surgery has proved disappointing except in a few instances. Hygiene and diet are generally considered as by far the most important factors in the general treatment.

Within the past few years, however, a number of highly specialized dietary procedures have gained unexpected prominence and apparently met with heretofore unmatched success. The first of these, primarily championed by Geyelin (M. Rec. **99**:1037, 1921) consists of somewhat prolonged starvation. The second method involves the use of strongly ketogenic diets, as advocated by Wilder (Mayo Clinic Bull. **2**:307, 1921) and Peterman (Peterman, M. G.: Ketogenic Diet in the Treatment of Epilepsy, Am. J. Dis. Child. **28**:28 [July] 1924) and reviewed some time ago in THE JOURNAL (J. A. M. A. **88**:1638 [May 21] 1927; **92**:1182 [April 6] 1929. Helmholz, H. F.: Ibid. **88**:2028 [June 25] 1927). All of these favorable therapeutic regimens, regarding the use of which many satisfactory reports are now available, have in common the development of a severe acidosis, which seems to be decisive in the prevention of epileptic seizures.

To these considerations McQuarrie (Am. J. Dis. Child. **38**:451 [Sept.] 1929) has added the significant observation that there appears to be a tendency for the epileptic subject to retain water during the active phase of the disease in amounts that are harmful. Convulsions tend to occur when a positive water balance above a certain magnitude is established. When diuresis follows the seizure, it favors the prevention of further seizures temporarily. Whether this effect of the extra water is due solely to changes within the brain cannot be said as yet. One is at once reminded of the phenomena described by Rowntree (Physiol. Rev. **2**:116 [Jan.] 1922) under the designation of "water intoxication." He has demonstrated that, when an intake of water is enforced in animals beyond the ability of the kidneys and other excretory channels to excrete the excess, profound symptoms ensue, including convulsions of cerebral origin and of extreme violence at times. The results can be accentuated when the water intake is attended with administration of such pituitary extracts as prevent the development of marked diuresis.

For the relief of the patient with epilepsy, McQuarrie has accordingly advocated marked restriction in the water intake, in view of the superficial relationship between water balance and the occurrence of seizures that has been determined under various conditions in a number of epileptic children at the University of Rochester, N. Y. He regards the etiologic factor in epilepsy as involving a sort of imbalance in the water metabolism—an upset between naturally occurring extrarenal processes of diuresis (dehydration) and antidiuresis (hydration). An analogous imbalance is known to occur in the case of diabetes insipidus but in an opposite direction from that which he postulates as being present in epilepsy. Experience in the clinic has demonstrated that procedures such as fasting, the use of ketogenic diets and stringent restriction of water with nonketogenic, borderline diets lead to partial dehydration of the tissues and prevention of seizures. Suddenly increasing the intake of water during the course of treatment by dehydration tends to cause recurrence of seizures, at least in the severe cases. Parenteral administration of solution of pituitary, or of the antidiuretic hormone of hypophysis, causes the development of a positive water balance and the occurrence of seizures in the epileptic subject. Urea in large doses causes loss of the retained water.

According to McQuarrie, the exact nature of the relationship of water balance to the occurrence of seizures is as yet quite obscure. It may be that the beneficial effect of partial dehydration depends merely on the mechanical relief from excessive pressure within the fluid channels of the brain. This would seem to be the most likely explanation in those patients having abnormal accumulations of cerebrospinal fluid in the subarachnoid spaces due to organic obstructions which interfere with normal absorption. For the other type of case, however, in which no such structural changes are found, explanation for the facts observed must be sought in a possible disturbance in the physiologic regulation of water balance within the brain. As McQuarrie further points out, the four different regimens that are known

to favor the prevention of seizures, namely, fasting, a ketogenic diet, rigid restriction of fluid intake and the administration of large doses of acid-forming salts, have in common the effect of dehydrating the tissues. It is true that these four procedures likewise tend to maintain the hydrogen ion concentration of the body fluids at a slightly higher level than would otherwise exist; but all the evidence so far obtained indicates that the relationship of any disturbance in acid-base equilibrium is of secondary importance. Within rather wide limits, McQuarrie concludes, procedures that tend to cause a shift in the acid-base balance toward the acid side favor loss of body water, whereas those causing a shift in the opposite direction probably favor retention of water within the tissues. This intimate relationship of the acid-base balance and the water balance makes it difficult to ascertain which is of primary importance, so far as the occurrence of seizures is concerned.

There are obvious advantages in employing a combination of restriction of water intake with a less rigorous ketogenic diet. The negative balance of certain elements, notably calcium and phosphorus, tends to become less; and the need for protein is not so accentuated as during a severe acidotic regimen. In any event, a disturbance in the water balance, perhaps affecting the central nervous system more specifically, appears to be closely identified with the etiology of epilepsy.

J. A. M. A.

THE LOCALIZATION OF VEGETATIVE CENTERS IN THE CEREBRAL CORTEX. FRANCISZEK WICHERT, J. f. Psychol. u. Neurol. **37**:693, 1929.

A girl, aged 14, was admitted to the hospital; her previous history, except for measles and pertussis in childhood, was unimportant. On admission, she said that suddenly and without apparent cause her right hand trembled for two minutes; she did not lose consciousness. On the next day, immediately after carrying a heavy barrel, the right hand began to shake again, after which she felt as if "something was running from the tips of the fingers to the throat"; at that time she was unable to speak and felt stiff; she was put to bed but did not lose consciousness; this attack lasted for about five minutes. Similar seizures recurred every three or four weeks, but at the end of six months they also began to involve the left hand, and later both lower extremities, more markedly on the right side. One year after the onset of the illness, the seizures became much more frequent and on several occasions were associated with loss of consciousness and biting of the tongue. At about the same time, the right hand became gradually weaker, and occasionally a series of attacks would be ushered in by minor attacks involving only the fingers of the right hand. Six months after the onset, the patient also noticed that on several occasions the attacks in the right hand would be preceded by cyanosis of the fingers, which began at the tips and was sharply limited at about the middle of the metacarpal bones; the cyanosis disappeared immediately after the attack. At about the same time, she also noticed that the cyanosis was associated with edema of the right hand which also disappeared with the cessation of the seizure. The right hand showed desquamation of the superficial skin and atrophy. The skin of this hand was smooth and shining, and was always warmer and more moist than that of the left. During the seizures the trophic and vasomotor disturbances were sharply separated from the adjacent normal skin. The right hand was thinner from the beginning of the illness. Roentgenologic examination showed the outlines of the bones of the right hand to be very distinct. The tendon reflexes on the right were always hyperactive and after the more severe seizures she would drag the right lower extremity. No pathologic reflexes were ever observed. The cranial nerves were normal except that following a series of attacks there was slight paresis of the right facial and oculomotor nerves which would soon disappear. The Wassermann reaction was negative in the blood and cerebrospinal fluid. Inoculation (intracutaneous and intraperitoneal) of a guinea-pig with cerebrospinal fluid gave negative results. The fundi were normal. Two years after the onset of the illness, the patient died in status epilepticus.

The mental examination revealed normal intelligence, memory, attention and behavior; just before the attacks she would become emotionally unstable and irritable with a tendency to depression and crying.

Microscopic examination showed diffuse changes in the ganglion cells throughout the entire central nervous system. These changes consisted of chromatolysis, disintegration of the intracellular fibrils and protoplasm with eccentric displacement and unusual dark staining of the nuclei. The predominant lesion in the cells was that of a severe degeneration. In the frontal lobe some areas showed acute cell disease (Nissl). In the left occipital lobe the changes in the second and fourth layers resembled those in the third and fifth. Ameboid transformation of the glia cells and an increased number of Hortega cells were in evidence everywhere. Fatty degeneration of the ganglion and glia cells and of the vessels was most evident in the cornu ammonis. Some parts of the cerebellum also showed an increased number of glia cells. Finally, the part of the motor cortex representing the right forearm showed an old scar 7 by 5 by 0.5 mm., consisting of glial and connective tissue fibers with an absence of ganglion cells and myelin fibers; in the area adjoining the scar, ganglion cells and myelin fibers were present but markedly diminished in number. There was no sclerosis of Ammon's horn. This scar, the author believes, was the anatomic substratum for the seizures and the diffuse changes in the ganglion and glia cells, the results of the seizures. The fact that this scar, which must have existed several years before the first seizures appeared two years before the examination, did not give rise to any clinical manifestations until that time, the author explains on the theory of changes in the body chemistry from the endocrine disturbances that must have existed at the time of puberty.

The history, clinical course and pathologic observations lead Wichert to believe that the case was one of symptomatic epilepsy following an old encephalitic process, perhaps in the course of the patient's measles or whooping cough. The vasomotor and trophic disturbances in the involved upper extremity are also attributed to the scar in the region indicated, and it is therefore concluded that special vasomotor centers for individual limbs and segments of limbs must exist in the cerebral cortex, especially in its deeper layers. The proof offered for this hypothesis, which has originally been presented by Monakow, is too speculative and not wholly convincing to the reviewer, especially as the author admits that the entire brain was not studied in serial sections.

KESCHNER, New York.

THE MICROSCOPIC CHANGES OF THE NERVOUS SYSTEM IN PSYCHOSES ASSOCIATED WITH PELLAGRA. A. Pentscheu, Ztschr. f. d. ges. Neurol. u. Psychiat. **118**:17 (Dec.) 1928

The brain possesses rather a marked resistance to the action of chemical agents. The true neurotropic toxins—botulism, tetanus, diphtheria, etc.—have little effect on the mind. Other toxins, such as alcohol, ether, chloroform, cocaine and morphine, produce severe mental disturbances which, however, last only as long as the toxin is effective. Only a few toxins can produce true psychoses over a long period (phosphorus, mercury, morphine, cocaine, absinthe, alcohol, nitrobenzol), but even in these it is found that with the progress of the poison there is a more or less rapid return to normal mental activity. In very advanced cases only do psychic symptoms persist, but these seldom develop to progressive psychoses. Only certain toxins constitute exceptions to this; these include lead, carbon monoxide and the alkaloid of *Secale cornutum*.

On the other hand, in pellagra, the brain is the least resistive organ in the body. Furthermore, the mental symptoms are progressive, and may begin when the other symptoms are at a standstill or have actually disappeared. In this respect pellagra differs from other exogenous toxins and shows certain similarities with some of the latent infectious diseases and endogenous psychoses.

Pentscheu reports seven cases of pellagrous psychosis in which mental symptoms were in the foreground. These patients died in a relatively short time. The

pathologic changes in the brain were as follows: (1) Inflammatory changes. These were present only in one case in the pons. (2) Fatty changes, which, however, are present in numerous other conditions. (3) Hyalinization of the capillaries and precapillaries in the superficial areas in the cortex; unpublished investigations by Klissurow show that these changes are found in many different conditions, even in the relatively young. It appears that the capillaries and precapillaries in certain areas of the central nervous system react to noxious agents by dilatation and hyalinization. (4) Ganglion cell changes, which are the most significant and which occurred in all seven cases. These are found in the macroganglion cells, and consist of a central neuritis or primary cell irritation. This pathology has been reported in all sorts of conditions—after cutting the axis cylinder, senile melancholia, endarteritis luetica, spastic pseudosclerosis, paresis, dementia praecox, Korsakow's syndrome, Landry's paralysis, etc. Though these changes are present infrequently in other diseases, they are constant in pellagra. They are infrequently found in areas outside the motor cortex, but in the latter place they are constant. The basal ganglia, midbrain, dentate nucleus, olives and Purkinje cells showed no changes of significance in the seven cases reported.

Pentscheu stresses particularly the changes in the spinal cord. A belief has arisen that the degenerations in the white matter are peculiar to pellagra. They occur in pernicious anemia, carcinoma, leukemia, tuberculosis and other diseases. "Pellagra is not a 'primary system disease of the spinal cord,' and further not a spinal cord disease at all, but rather a disease in whose later stages the cerebrum is involved. The not infrequent disease of the spinal cord, which is often lacking completely, has nothing at all to do with the cause of pellagra, but is caused by the nutritive disturbances accompanying the disease."

Pellagra is not an inflammatory disease. It is much like two other conditions which cause mental symptoms after a period of latency—lead and carbon monoxide. Pellagra, says Pentscheu, is a disease which produces an "angiogenic psychosis," so that one must assume that the pellagra toxin has a vessel-injuring component.

ALPERS, Philadelphia.

THE CEREBROSPINAL FLUID, THE ANATOMY OF THE SUBARACHNOID SPACE AND THE BARRIER BETWEEN THE BLOOD AND CEREBROSPINAL FLUID. L. L. PAPADATO, Collected Papers, Neurological Clinic, State Medical Institute, Odessa, U. S. S. R. **19**:99, 1929.

In a prolonged article, the author gives a complete review of the work and literature of Russian and foreign investigators in regard to the whole subject of cerebrospinal fluid. Embryologic and physiologic data point to the conclusion that the choroid plexus has a secretory function. If this is so, then the question of innervation naturally arises. An investigation of this problem consisted in a series of experiments in which the central ends of the cervical sympathetic fibers were stimulated. In the first series of experiments the internal carotid sympathetic plexus was stimulated. In the second series the central end of the vagosympathicus was stimulated, and in the third series the vagus was stimulated after it had been cut and the central nerve fibers had been allowed to degenerate.

In the first series of experiments dogs were anesthetized, and the plexus lying over the carotid artery was exposed. A cistern puncture was done at the same time. The proper location of the plexus was ascertained by stimulation of the sympathetic to see if there was dilatation of the pupil. As soon as a normal rate of flow of the spinal fluid began the experiment was commenced. A small electrode was applied to the plexus. A Dubois-Raymond coil was used with a current discharging from one dry cell. As a result of irritation of the sympathetic nerve fibers, there was a marked increase in flow of the cerebrospinal fluid. The rate of the flow was recorded automatically by a small moving picture camera.

As there is a great deal of uncertainty in locating the plexus and the whole operation is technically difficult, the second series of experiments was undertaken in which the vagus-sympathicus was exposed and the central fibers were stimulated. As in the previous experiment, a cistern puncture was done. The central ends of the sympathetic nerve fibers were stimulated by a very weak faradic current. The rate of flow was in an inverse ratio to the length of the experiment. With the electrical current, during the period of irritation and also afterward. The rate of flow was in an inverse ratio to the length of the experiment. With irritation of the central nerve fibers there was an increase in the rate of flow of the cerebrospinal fluid, but with each succeeding irritation the flow was less and less. Thus in the beginning of the experiment a drop came out about every thirty-seven seconds, while toward the end of the experiment it took on an average two hundred and forty-eight seconds for each drop of fluid to appear.

The author comes to the conclusion that the irritation of the cephalic end of the vagus-sympathicus leads to an increase in the cerebrospinal fluid pressure with increase in the rate of flow. This is due to the sympathetic nerve fibers because when the influence of the sympathetic is eliminated by allowing them to degenerate these phenomena are not observed. The author also concludes that the increase in the cerebrospinal fluid pressure is due in the experiments to the increased secretion of the choroid plexus. The sympathetic nerve fibers are the secretory nerves of the choroid plexus.

KASANIN, Boston.

THROMBO-ANGIITIS OBLITERANS, Editorial, J. A. M. A. **93**:1891 (Dec. 14) 1929.

A malady of the blood vessels and circulation described as obliterating endarteritis has been recognized for half a century or more. In 1908, Leo Buerger of New York clearly differentiated a clinical and pathologic entity characterized as an inflammatory disease involving the deep-seated arteries and veins and the superficial veins of the extremities. This is today known as thrombo-angiitis obliterans. In the early stages of the process a thrombus develops; this later undergoes organization or healing, with ultimate complete occlusion of the affected vessels. The assumed association of Buerger's disease with blood vessels of the extremities is widespread. According to studies of Barron and Linenthal (Thrombo-Angiitis Obliterans, Arch. Surg. **19**:735 [Oct.] 1929) in Boston, however, thrombo-angiitis obliterations should not be regarded as involving the vessels of the extremities exclusively. In fact, they aim to direct attention to the more general distribution of the disease in contradistinction to what has previously been believed concerning it. Barron and Linenthal assert that the malady attacks the walls of the blood vessels, both veins and arteries, throughout the entire vascular system, the cranial, thoracic and abdominal vessels as well as the vessels of the extremities. The signs and symptoms are characteristic of the vessels involved, so that the lesion affecting the arteries of the brain may give rise to a hemiplegia of varying degrees of severity; or, should the coronary vessels be involved, the characteristic symptoms of coronary thrombosis or angina pectoris may ensue. The Boston study reminds one of the description of the chronic disease process as a race between the formation of a collateral circulation and the occlusion in the main arterial channels. It is further pointed out that the vessels involved are slowly occluded and, owing to this slow occlusion, there is an opportunity for collateral circulation to be established. This explains the fact that the nutrition of the part supplied by the occluded vessel is maintained, and a patient may go on for many years without nutritional disturbance of the parts involved. The process in the arterial tree does not spread by extension from a single focus but may occur at different levels in an artery and in various vessels at different periods. Thrombo-angiitis obliterans thus becomes "a generalized disease that may affect any part of the arterial tree, including the coronary arteries, the abdominal arteries and the arteries of the brain." Accordingly the occasional cases of angina pectoris and coronary thrombosis that occur early in life without any evidence of vascular disease elsewhere may, in some instances at least, be due to thrombo-angiitis obliterans of the coronaries and not to arteriosclerosis.

J. A. M. A.

THE PRECIPITATION OF ENDOGENOUS PSYCHOSES BY EARLY PARETIC BRAIN PROCESSES AND THE SIGNIFICANCE OF THEIR COURSE FOR THE PROGNOSIS OF PARESIS. A. BOSTROEM, Arch. f. Psychiat. **86**:151 (Jan.) 1929.

The author starts with the recently published observation of Spielmeyer in cases of early paresis. These show that histologic changes of the type belonging to early paretic processes may occur without any concomitant clinical signs. The absence of mental symptoms of the disease in such early cases is especially stressed. The occurrence of such a process in persons who had predispositions to some form of endogenous mental disease may, according to the author, precipitate such a psychosis. The two most important forms of endogenous psychoses — manic-depressive psychosis and schizophrenia — are discussed. He cites the history in five cases that undoubtedly had the essential features of a cyclothymic make-up and which in the very early stages of the paretic process, presented more or less typical manic-depressive episodes. The fact that the psychosis was mostly an expression of the endogenous predisposition and was precipitated only by the paretic process was further proved when the psychosis cleared up on the administration of malarial treatment without leaving any defect. Two cases of schizophrenic psychoses precipitated by paresis are also reported, and here, too, one finds that the persons had shown definite tendencies to schizoid manifestations even before the onset of the psychosis. The mental disturbance itself was characterized by the essential features of schizophrenia, and after a successful administration of malarial treatment no signs of a paretic type of defect were left, but the patient still showed the symptoms of schizophrenia.

The author is of the opinion that in numerous instances the organic changes in the brain in their early stages may run their course without any psychic manifestations. When there is a predisposition to some form of psychosis, they help to precipitate it, but when this takes place, the psychosis is really endogenous, and treatment, especially in the manic-depressive types, will be of great value and of a good prognosis. There are, however, paretic processes, especially in the late stages, in which the mental symptoms are produced by the organic changes in the brain. Here, too, the type of personality will color the behavior, but the important cause will be the organic change. This is mostly found in cases that have run a long course and in which treatment is not so promising.

MALAMUD, Foxborough, Mass.

THE IRRITABLE COLON. Sarah M. Jordon and Everett D. Kiefer, J. A. M. A. **93**:592 (Aug. 24) 1929.

Irritable colon is a condition wherein the musculoneural apparatus of the colon has lost its coordination and correlated function. Colitis is a poor term as there is no inflammation. Irritable is also inadequate as in many cases irritability is decreased rather than increased. The condition consists of disturbance in the propulsion of colonic contents from cecum to rectum, the reabsorption of fluid and the digestion of cellulose. Delayed or increased motility, excessive or subnormal absorption of fluid and imperfect digestion of cellulose cause the patient to become conscious of some abnormality in digestion.

In a series of 3,000 admissions to the gastro-intestinal service of the Lahey Clinic, 30 per cent were found to have no lesion other than this colonic musculoneural disturbance. The diagnosis is made on the basis of symptoms, generalized abdominal tenderness and exclusion of other abdominal pathologic change and on roentgenologic observations in the colon.

The authors present a series of 200 cases chosen at random and studied with regard to symptomatology and roentgenologic observations. The symptoms may be divided into three groups: gastro-intestinal, cardiorespiratory and nervous.

The roentgenologic diagnostic criteria are: (1) the length of the colon and the presence or absence of redundance; (2) the rate at which the colon fills and empties; (3) the appearance, depth and frequency of haustral markings; (4) the diameter under certain pressure and with filling of the cecum, and (5) the absence of sensation or the occurrence of distress during the passage of the enema. Comments are made, tables are presented and roentgenograms are illustrated.

The authors conclude that: (1) irritable colon occurs frequently in patients complaining of digestive symptoms; (2) the opaque enema is of diagnostic value as well as affording a check-up on treatment; (3) symptoms of intra-abdominal organic lesions, cardiac disease and systemic nervous disorders are seen in association with this condition; (4) the effective treatment for hypo-irritability or hyper-irritability is rest, generally and locally to the colon, bland diet, heat, omission of catharsis, and atropine.

CHAMBERS, SYRACUSE, N. Y.

THROMBO-ANGIITIS OBLITERANS. (EXPERIMENTAL REPRODUCTION OF LESIONS.) LEO BUERGER, Arch. Path. **7**:381 (March) 1929.

Buerger originally expressed the belief that the acutely inflamed veins and nodosities of thrombo-angiitis obliterans could furnish the material in which an infectious agent-virus or micro-organism might reside and be brought to light; and secondly, that these foci might be utilized for the reproduction of the disease or, at least, of some of the acute lesions of the malady. With this in mind he conducted researches along these lines, but with little success. Having failed to discover the micro-organism he turned his attention to the reproduction of the acute lesions. He was able to reproduce lesions identical with those of acute thrombo-angiitis obliterans, acutely inflamed veins with miliary giant cell foci, in the superficial veins of the upper extremities of man, by transplantation of the coagulated contents of acutely affected veins when in the phase of migrating phlebitis.

The method of procedure was to ligate doubly a vein, including between the ligatures from ½ to 1 inch or more of its length, without disturbing its continuity. These experiments were conducted in persons without vascular disease — persons with thrombo-angiitis obilterans and also persons with moderately pronounced arteriosclerosis — a vein of the forearm being used in each case. The injection was made of material from the veins in an acutely migrating case of thrombo-angiitis obliterans. This method resulted in failure. Another method of introduction of the material was therefore devised, scrapings from the adventitia of the involved vessel being used, and the adventitia of the experiment vessel being traumatized. In the latter experiments, when the veins were excised from nine to twelve days after the implantation lesions practically identical with those of acute thrombo-angiitis obliterans were found; namely, a diffuse polymorphonuclear infiltration of the wall of the vein and a clot containing typical miliary giant cell foci. In his conclusion Buerger states that the paravascular implantation of clot from cases of acute thrombo-angiitis obliterans was followed by the development of typical lesions in the apparently healthy ligated veins of the person who had received inoculation.

WINKELMAN, Philadelphia.

RIGIDITY ORIGINATING IN THE OLIVES: DISCUSSION OF A VASCULAR LESION OF THE LEFT INFERIOR OLIVE WITH SECONDARY ATROPHY OF THE RIGHT OLIVE. G. GUILLAIN, P. MATHIEU and I. BERTRAND, Ann. de méd. **25**:460 (May) 1929.

A man, aged 57, developed bulbar symptoms after a transitory hemiparesis: difficulty of deglutition and phonation, hypesthesia of the face and difficulty in hearing. The tendon reflexes were lively; there was a certain slowness of movements. Gradually, within two years after the onset, generalized rigidity developed; it was more marked than rigidity observed in the postencephalitic parkinsonian syndrome. The rigidity was associated with catatonia and a tremor of the upper extremities, which was regular in rhythm and of short amplitude. The autopsy, following death from bronchopneumonia, revealed a small area of softening extending through the lower half of the left inferior olive. The upper half was grossly intact but the lateral third of the medulla oblongata posterior to it was also destroyed. The pyramids and the arcuate nuclei were not affected. The right olive presented the picture of mild atrophy with sclerosis. The right restiform

body was reduced in size and not as well myelinated as the left. Serial sectioning revealed a second focus of softening in a section through the lower border of the pons. Mesially it touched the right medial lemniscus and laterally it destroyed the fibers of the anterior spinocerebellar tract, together with some transverse pontile fibers. No histologic changes of the nuclei of the midbrain were found.

The authors refer to cases of olivopontocerebellar atrophy and hereditary cerebellar ataxia with rigidity. Such cases are cited to support their theory that the rigidity in the case they report was due only to the destruction of both olives. In their opinion these two structures form an important nucleus intercalated between the nuclei of the mesencephalon and diencephalon, on the one hand, and the cerebellum on the other. The olives regulate the tonus of striated muscles and are responsible for erect posture. The studies of N. Zand are cited to prove, from comparative anatomic studies, that in members of the same order the olives are best developed in the animal with erect posture. The olives obtain their maximal development in man. In the final conclusions, it is emphasized that all components of the parkinsonian syndrome — rigidity, tremor and hypokinesis — may be produced by a localized lesion of the inferior olives.

WEIL, Chicago.

MUSCULAR DYSTROPHY FOLLOWING ENCEPHALITIS. PAUL SCHILDER and MAX WEISSMANN, Med. Klin. **25**:748 (May 10) 1929.

The writers report the cases of two patients who developed a muscular dystrophy following encephalitis:

CASE 1.—A man, aged 25, who had encephalitis in 1921, recently had observed weakness in the arms, especially on the right side. There were no other complaints. On examination, he presented some of the psychic disturbances noted with post-encephalitic sequelae. The general physical examination gave negative results. Neurologic study showed hypertrophy of the shoulder girdle muscles, more especially on the right side and involving the deltoid muscle. These muscles felt leathery and, in spite of their size, were weak. The reflexes were normal, and there was no myotonic reaction.

CASE 2.—A boy, aged 19, had had severe encephalitis eight years previously. About one and one-half years ago, he first observed a change in gait and later an increase in the size of the left thigh. General examination gave negative results. He, too, presented some mental changes. Neurologically, he was muscular, but the left thigh and the right shoulder girdle muscle were distinctly hypertrophied. All his muscles felt hard and firm. On testing the power of any single muscle there was no apparent loss of strength, but the gait was distinctly waddling in character. The reflexes were normal, and the electric reactions were unaffected. He presented a slight tremor about the mouth.

The writers point out that there was little question regarding the encephalitis. Both patients were young men, and the family histories were entirely negative for any similar disturbance. According to the writers, it seems possible that the encephalitis affected trophic centers in the midbrain. Westphal observed four patients with juvenile progressive muscular dystrophy in conjunction with extrapyramidal disturbances, of choreiform, athetoid and myoclonic character. Sträussler and Kuré have made somewhat similar observations, though they attribute the muscular disturbance to lesions of the sympathetic and parasympathetic muscle centers in the midbrain. It would seem from the present observation that there may exist a trophic muscle center in the diencephalon.

MOERSCH, Rochester, Minn.

INHIBITORY EPILEPSY. S. A. KINNIER WILSON, J. Neurol. & Psychopath. **8**:332 (April) 1928.

The fact that many of the phenomena of what is ordinarily understood as epilepsy are inhibitory and not excitomotor has scarcely received the attention it deserves. Loss of consciousness is an arrest of function. The most typical feature

of petit mal is cessation of function of one form or another. Gowers alluded to the possibility of sensory stimuli being succeeded not by motor excitation but by motor inhibition. Wilson describes in detail a patient who was observed for several weeks but was then lost track of. For about fifteen minutes there was an aura which consisted of "mistiness of the eyes" and "bright flashing stars" when looking to either side; this was followed by tingling in the left hand, arm, trunk, leg and toes, in that order, and finally in the left side of the lower part of the face and in the tongue. This sensory phenomenon lasted for only a few seconds or minutes and was followed by numbness and total loss of power in the same areas for from one to twenty minutes. Headache without nausea or vomiting might last for a day afterward. Examinations were made during three attacks. The limbs were flaccid at first; this was followed by a period of relative rigidity. During the process of recovery from the stage of absolute flaccid akinesia, the limbs for a time exhibited the phenomenon of defective inhibition of the antagonists. The author has noted this abeyance of Sherrington's law of reciprocal innervation in chorea and athetosis. Such interference is commonly cortical. The sensory phenomena in this case were necessarily cortical in origin. Exaggerated reflexes and ankle clonus, which are present in the stage of rigidity, point to infracortical release synchronous with cortical inhibition. The temporary motor paralysis without spasmodic discharge must be ascribed to inhibition of motor centers. Other instances of powerful stimulation leading to arrest of function are cited. One may readily conceive of a refractory or inhibitory phase developing in a motor mechanism if it is suddenly or rapidly assailed with violence by afferent stimulations of an exaggerated character. Epilepsy cannot call into being physiologic processes that do not exist. At the most it can only distort or caricature the processes that are present.

FAVILL, Chicago.

FATIGUE OF THE SENSE ORGANS IN MUSCLES. D. W. BRONK, J. Physiol. **67**:270 (June) 1929.

This investigation by Bronk is devoted to a study of the action of peripheral sense organs during and after a prolonged response to a continuing stimulus. The preparation employed was the flexor superficialis muscle with the tibialis superficialis nerve. All of the experiments were made on noncirculated, excised tissue.

The author found that the rapid adaptation of the end-organs was followed by a more gradual decrease in the frequency of their impulse discharge. He attributed the latter decrease to fatigue. The greater the tension applied to the muscle the greater is the decline in frequency, with the result that after some minutes of a sustained tension the frequency of afferent impulses was less under the stronger stimulus. There was partial recovery from the fatigue under a lower tension, the reduction in the stimulus causing an increase in impulse frequency.

Bronk thinks that the decrease in frequency during a prolonged stimulus is due, in part, to the fact that progressively fewer end-organs discharge as the stimulus continues. An investigation of single end-organs showed that as they fatigued the frequency of their discharge fell. This decrease in discharge frequency in some preparations resulted from a gradual and continuous transition from a high to a low value. More often, as the frequency fell, more and more impulses dropped out of an otherwise fairly regular series.

The author noted that muscles could be stretched more than 1,000 times with only one second intervals of rest without showing any appreciable fatigue, provided the successive stretches were of short duration. If, however, the duration of the tension was prolonged for several minutes the response to a subsequent stretch was greatly reduced. He also found that the discharge frequency declined more and more rapidly with fatigue.

Experiments conducted to observe the effect of loading a muscle in an atmosphere of nitrogen showed that it hastened fatigue of the sense organs and retarded recovery. Oxygen had the opposite effect.

ALPERS, Philadelphia.

SOME FACTORS THAT INFLUENCE THE INCIDENCE OF TYPES OF PHYSIQUE IN SCHIZOPHRENIC, CRIMINAL AND NORMAL PERSONS. A. PERELMANN and S. BLINKOW, Arch. f. Psychiat. **86**:501 (March) 1929.

The occurrence and relative proportions of the Kretschmer types of physique in more than 900 persons are reported. The group consisted of 690 men and 213 women of different nationalities (Russians, Armenians, Turks, Jews, etc.). There were 100 schizophrenic patients, 463 criminals and 340 mentally normal persons. Following are the conclusions:

The persons with schizophrenia are mostly leptosomes. Some of them are athletic and dysplastic, and a few are pyknic. The latter form an especially small proportion of the male cases, whereas there are more of them in the female. This is also true of the dysplastic type. The persons with schizophrenia, furthermore, show a surprisingly large number of pure types, there being few indefinite and atypical forms in this group. The criminals, and especially murderers, show a surprisingly high preponderance of the athletic type, this being true of both males and females. This fact would tend to corroborate the statements made by other authors that the athletic type corresponds to a certain psychic make-up (such as the epileptoid constitutional type). There is special and fairly definite relationship between sex and the incidence of physique types. Thus, the pyknic type is found more frequently among women, whereas there are more of the athletic type, leptosomes and mixtures of these among men. The age of the person influences the incidence of types so that there are more of the pyknic type after the age of 30 than before. Such an influence is also exerted by the race of the person; thus, there are more of the pyknic type among the Russians and a preponderance of leptosomes and of the athletic type in the Persian Turks. The authors do not agree with the statements made by some investigators that the incidence of the physique types in schizophrenic persons are the same as in normal persons. He finds that there is a definite preponderance of leptosomes and athletic types in patients of schizophrenia, a preponderance which is far beyond the proportions found in normal persons. The low incidence of the pyknic type among persons with schizophrenia is especially accentuated in the case of Russian patients, who, under normal circumstances, show a high proportion of the pyknic type.

MALAMUD, Foxborough, Mass.

PROGRESSIVE HYPERTROPHIC INTERSTITIAL NEURITIS. ARTHUR SLAUCK, Klin. Wchnschr. **8**:927 (May 14) 1929.

The purpose of this article is to call attention to the fact that a deformed foot may not be primarily an orthopedic problem but may be primarily the result of a neural change. It is advisable, therefore, before doing tenotomies or tendon transplants to ascertain whether the underlying trouble is not of a neurologic character. In 1912, Johannes Hoffman described the picture of progressive hypertrophic neuritis and showed that the condition consisted of a primary degeneration of the sheath of Schwann with secondary degeneration of the myelin and axis cylinders, which process tended later to ascend and involve the cord. The clinical picture is one of a chronic polyneuritis with loss of reflexes, muscle atrophy, electrical changes and sensory disturbances in the distal portion of the limb. It is noteworthy that a familial tendency to gait disturbance or foot deformity exists and that the general appearance of a foot is similar to that seen in progressive muscular atrophy or even Friedreich's ataxia. The nerves are thickened, hard and painful, and usually all peripheral nerves are involved to some degree.

Slauck reports the cases of a father and a son. The father, aged 34, said that his father and one sister were similarly affected; he himself had had trouble as long as he could remember, though the deformity never caused him much difficulty. Examination showed a high arched foot with lost achilles and patellar reflexes. The peripheral nerves were thickened, and there was diminution of electrical responses. The feet showed symmetrical atrophy, but there were no fibrillary twitchings and sensation was intact.

The son, aged 4, from early childhood presented high arched feet with rather large insensitive nerves. This insensitiveness of the peripheral nerves is so marked that the patient will complain but little when the supra-orbital nerve is stimulated with an electric current. This point alone will usually establish the diagnosis in a doubtful case.

MOERSCH, Rochester, Minn.

DOES THE TUBER CINEREUM CONTAIN THE VASOMOTOR CENTERS OF THE KIDNEYS? N. N. SIROTININ, Med.-biol. j. **5**:85, 1928.

A great deal of work has been done in the localization of the vasomotor centers for various organs. It has been accepted that the main vasomotor center is in the medulla about 3 mm. above the calamus and extending to the lower edge of the pons. A definite relationship of the tuber cinereum to water metabolism has been observed.

In order to investigate the cause of polyuria in its relationship to the tuber cinereum the following experiments were conducted. A dog was anesthetized under morphine-chloroform anesthesia. A laparotomy was done, one kidney being exposed, and an oncometer applied to the kidney. A recording device connecting the oncometer with a kymograph was provided. A craniotomy was done, and the base of the brain exposed. The blood pressure was recorded by introducing a cannula into the femoral artery, transmitting the variations in pressure to a recording device.

When a 60 per cent solution of potassium hydroxide was applied to the tuber the results were variable, probably because the chemical penetrated the tissues and destroyed them. The same uncertain results were obtained with chloroform. When a weak inductive current was applied, a slight elevation of blood pressure resulted with increase in the volume of the kidney. These results were obtained when all parts of the tuber cinereum were stimulated, although minor variations were noted. When all the visible nerve fibers to the kidney were severed the same results were obtained, although in a lesser degree. This was due to the fact that a complete denervation of the kidney is impossible because the blood vessels carry some of the nerve supply. However, when this was attempted by cutting the renal artery (permitting the blood to circulate through a cannula) stimulation of the tuber did not result in subsequent enlargement of the kidney, although the blood pressure was somewhat raised.

As a result of his experiments the author believes that polyuria is due to vasomotor changes. There is no evidence at present of the existence of any special secretory centers.

KASANIN, Boston.

FEVER THERAPY IN SCHIZOPHRENIA (SAPROVITAN). G. BLUME, Arch. f. Psychiat. **86**:790 (March) 1929.

The author introduces the discussion of his results by a review of fever therapy in mental diseases in general. The promising results of the treatment for paresis have suggested similar methods of approach in the treatment for other mental diseases. Twenty-six patients were selected; they were all women, aged from 15 to 30 years, and presented a more or less similar mental picture: catatonic dementia praecox. A similar group consisting of twenty-five cases was under observation as a control.

The results were as follows: Nine of the patients showed what the author considers a complete remission and so far have not shown any tendency to a relapse. These patients were all allowed to leave the hospital and are getting along well outside. The patient in the oldest case has been out for two years. Six of the patients showed definite improvement, but were still unable to take up their previous social level. Most of them have been dismissed, under supervision, to be seen only on visits to the hospital. Two of the patients showed a temporary remission following the treatment, but then there was a relapse. Nine patients were not affected by the treatment, the condition remaining either the same as before treatment or worse. One of these patients died of pulmonary tuberculosis, and it is probable

that the rather radical treatment was responsible for an acceleration of the process. The author states that in choosing the material for treatment one should eliminate cases that show physical contraindications. In comparing these results with the control material, one finds that of twenty-five cases, only four showed a good remission, six a moderate remission and fifteen no change. It is interesting to note, too, that the remissions in the patients treated occurred earlier in the course of the disease than they did in the few cases among the controls in which the patients showed improvement. The proportions of improvements in the patients not treated are in accord with those given by Kraepelin and other authors. In conclusion, it is thought that fever therapy in schizophrenia holds out good promise; further investigation of its effectiveness should be undertaken.

MALAMUD, Iowa City.

UNUSUAL SYMPTOMATOLOGY AND COURSE IN ENCEPHALITIS IN CHILDREN. Fritz von Bermuth, Ztschr. f. d. ges. Neurol. u. Psychiat. **118**:234 (Dec.) 1928.

Bermuth reports three cases of encephalitis in children, the first two in a brother and sister. The first case was in a boy, aged 2¾ years, who was taken suddenly ill with vomiting and an inability to walk or stand. In addition, he had a left abducens paresis, nystagmus, especially on looking to the left, conjugate gaze to the right, increased tendon reflexes and a positive Babinski sign. A left cerebellar localization was made and tumor suspected, but in view of the rapid onset, the rapid disappearance of all signs in a relatively few days and the hypersomnia, a diagnosis was made of encephalitis involving the pons and the floor of the fourth ventricle, a diagnosis which seemed to be supported by case 2, who was a sister of the first patient. This patient was a girl, aged 6, who was suddenly taken ill with vomiting, frontal headache and complete amaurosis without fever. The pupillary reactions were normal; the patella and achilles reflexes were difficult to obtain, and the eyegrounds showed a marked choking of the disks. Lumbar puncture gave normal results, with a pressure of 190 mm. of water, but cistern puncture showed a markedly increased pressure. Because of this and the complete blindness which had to be attacked in some way, the ventricles were emptied. A few days later, the child could count fingers, and in the course of a week vision had returned to 5/20 and 5/15. Though tumor was suspected, a diagnosis of encephalitis was made, with edema of the brain and a blocking of cerebrospinal fluid. The third case concerned a child, aged 8, who had an encephalitis following an attack of measles. After eight weeks, she recovered, but developed a character change characterized by lying and stealing. The mentality was decreased. During the course of a year the behavior disturbances disappeared, the mental deficit cleared up and the child became again normal. This case of metencephalitis was considered exceptional in its course.

ALPERS, Philadelphia.

THE VESICAL NERVE PLEXUS IN THE CHICK EMBRYO. Z. SZANTROCH, J. f. Psychol. u. Neurol. **37**:679, 1929.

The fact that the cloaca in the chick is a part of the intestinal canal, as well as the fact that its smooth musculature and its corresponding nerve formations are developed along the same principles as the other parts of the gut, justify the inclusion of the vesical nerve plexus in the nervous system of the intestine. This, however, is made up of various components, i.e., from outer and inner parts, depending on whether they are differentiated from the outer or from the inner part of the main musculature (circular muscle layer). Among the outer parts one must again distinguish between the primary and secondary nerve formations. The primary may remain permanently as nerve networks in the wall of the gut (esophagus, stomach, caudal limb of the duodenum), or they may form the nervus intestinalis outside the wall of the gut. Where the primary nervous system leaves the wall of the gut — in the region of the intestinal nerves — there is formed the secondary outer nervous system. The inner nerve plexus is chiefly developed only

in the mid and hind intestine. The question now arises: To which one of these nerve formations in the intestinal wall does the vesical nerve plexus belong? The vesical nerve plexus develops at the same time and from the same matrix as the circular musculature of the gut. (This can be especially seen in the allantoic stalk.) It is, therefore, equivalent to the primary intestinal nervous system. This again raises the question whether this plexus can be compared with the nervus intestinalis or with the primary nerve network. Szantroch believes that the vesical plexus assumes an intermediate position between these structures. The reasons for this opinion are: 1. The vesical plexus remains permanently included between the circular and longitudinal musculatures. 2. It has a definite tendency to form solid nerve strands which resemble the nervus intestinalis.

KESCHNER, New York.

MODE OF INHERITANCE OF REACTION TIME AND DEGREES OF LEARNING IN MICE. E. M. VICARI, J. Exper. Zool. **54**:31 (Aug. 5) 1929.

The manner of inheritance of four lengths of reaction time and of four degrees of learning, measured in a simple maze, of four stocks of mice involving around 900 individuals, was studied. Three crosses made from four closely inbred stocks were studied. Reaction time was found to be the best criterion to measure the maze learning response. Though difficult of handling, the response reaction time can be studied from the mendelian point of view. Short reaction time can be considered as a character versus long reaction time. When there is a wide difference between the two characters, some form of dominance of the short reaction time is evident. When there is a small difference the hybrid is superior over each parent's reaction time. This might be attributed to hybrid vigor or heterosis, and may be explained by recombination of several factors in the F_1 hybrid which were present in the two parents. This view is favored by the wider variability and intermediate position of the F_2 generation. The degree of maze learning, expressed in terms of the number of perfect runs and the largest number of consecutive perfect runs, behaves in the same way as reaction time. The factor or factors responsible for the behavior response reaction time may be identical with the behavior response degree of learning, since the method of inheritance of the two responses is the same. Family studies confirm in every way the group studies of each cross. Subsequent generations show no indications of having been aided in learning a simple maze problem by the training of three generations of ancestors. No evidence, therefore, for the inheritance of acquired characters was seen.

WYMAN, Boston.

FAMILIAL SHORTENING OF THE METACARPAL BONES AND SCHIZOPHRENIA. D. MISKOLOCZY, Arch. f. Psychiat. **87**:242 (May) 1929.

In a case of paranoid dementia praecox the author found marked shortening of the third and fifth metacarpal bones of both sides. This anomaly was externally manifested by shortening of the middle and little fingers of both hands (the middle finger was 7 mm. shorter than the ring finger). An investigation of the family history with this in view brought the following results:

Anomalies in the development of the metacarpal bones were traced to the third generation, all on the maternal side of the family. The grandfather of the patient is said to have had shortening of the fifth metacarpal on both hands. All of his children but one showed anomalies of this kind, although more than one metacarpal bone was involved. The patient's mother was the first to show involvement of the fifth and third metacarpals (similar to the patient). In the third generation, the patient was the only one who showed this anomaly. With the somatic stigmas there was a distinct tendency to schizoid behavior, although the patient was the only one who developed a definite psychosis. An interesting factor in the clinical picture was the tendency to weave the somatic deformity into the paranoid trend. The patient believed that the mother had caused this deformity by an injury in early life; later, the patient developed the idea that she had taken revenge on the

mother by deforming the latter's hands. A discussion of the possible mechanisms suggested in this picture follows the presentation of the material, and the author lays especial emphasis on the fact that there is here a combination of development anomalies in the mesenchyma and in the ectoderm.

MALAMUD, Iowa City.

ISOLATION AND CULTIVATION OF THE MENINGOCOCCUS: A SIMPLE ROUTINE METHOD. Ruth Gosling, J. A. M. A. **93**:611 (Aug. 24) 1929.

Motivated by the difficulty experienced by many laboratories in isolating the meningococcus from the cerebrospinal fluid of patients with epidemic meningitis and in keeping the strains alive without frequent transplanting, the author describes the method used by the meningitis division of the New York City Health Department. All cloudy or hazy fluids are subjected to the following routine. All specimens are centrifugated at high speed for from five to ten minutes. The fluid is used for chemical examination and the sediment for smears and cultures. The first specimen is planted on coagulated blood agar slant, streaked red blood plate, plain agar slant, nutrient broth and a dextrose semisolid tube. With the last the material is thoroughly blended into the upper half inch of the medium. In the last the highest percentage of meningococcus growths occurs. Its composition and preparation are described. The meningococcus appears in from eighteen to ninety-six hours. The cultures may be kept for two and one-half months or more.

Using this medium, eighty-one positive cultures out of eighty-nine consecutive fluids were obtained. Five of the eight cases in which no growth was obtained showed an occasional organism in the smear. Seven positive growths were obtained from ten fluids exhibiting no organism in the smear.

CHAMBERS, Syracuse, N. Y.

MYELO-ARCHITECTONIC STRUCTURE OF THE PORTION OF THE TEMPORAL LOBE LYING WITHIN THE SYLVIAN FISSURE IN THE CHIMPANZEE (TROGLODYTES NIGER). EDUARD BECK, J. f. Psychol. u. Neurol. **38**:309, 1929.

A reconstruction of the temporal lobe in the chimpanzee showed a remarkable resemblance to that of man. Although the size of the surface in the latter is much greater, nevertheless it is not even double the size in the former. The divisions of the gyri and sulci of the chimpanzee's temporal lobe are approximately the same as those in man. As in man, so in the chimpanzee no difference could be made out between the right and the left hemispheres.

Architectonically, there is no difference between the regions, subregions and their divisions (partes) in the chimpanzee's temporal lobe and that in man, except that in the latter the regio entorhinalis is displaced into the mesial surface of the temporal pole. There is, however, a considerable difference in the amount of white substance, of which there is much less in the chimpanzee, especially of the ground-fiber network.

In view of the fact that the left hemisphere does not differ architectonically from the right, one may definitely conclude that both hemispheres have the same function. For myelo-architectonic as well as architectonic reasons one may also conclude that the central auditory region is located in the temporal transverse regions and reaches as far as the mesial fields of the subregio temporalis transversa secunda, although the latter subregion may have some relation to central audition. In this respect the temporal lobe in the chimpanzee does not differ materially from that of man.

KESCHNER, New York.

THE HYPOPHYSIS OF THE PORPOISE (TURSIOPS TRUNCATUS). GEORGE B. WISLOCKI, Arch. Surg. **18**:1403 (April) 1929.

A careful description is given of the hypophysis of a porpoise. In the porpoise the processus infundibuli is separated anatomically from the buccal portion of the hypophysis by a fold of dura, a portion of the diaphragma sellae. The pars

intermedia and hypophyseal cleft are completely lacking in the adult porpoise, the pars buccalis consisting solely of a pars tuberalis and a pars distalis. The pars distalis consists of lobules which are much more pronounced than in other mammals. These lobules contain three types of cells similar to those customarily recognized in the mammalian hypophysis. With Mallory's connective tissue stain, however, many of the basophils and a few of the eosinophils contain both acidophilic and basophilic granules. These cells suggest transitional forms between basophils and eosinophils. Within each lobule the cells are arranged in a somewhat definite relationship. The periphery or rim of each lobule is formed solely by a row of granular cells, whereas the center of the lobule consists chiefly of chromophobe cells, besides occasional eosinophil, basophil or fat cells. The pars tuberalis is composed of follicles containing colloid. The epithelial cells lining the follicles are chromophobe and usually in single layers. The pars nervosa is composed throughout of neuroglial tissue, supporting blood vessels. Nerve cells, hyaline bodies or droplets of colloid are not present. The infundibular cavity does not penetrate the processus infundibuli.

GRANT, Philadelphia.

REACTIVE AND CHARACTEROLOGIC FACTORS WITH PHASIC AND PROCESS-LIKE COMPONENTS IN PARANOID DELUSIONS: "SENSITIVE REFERENCE PSYCHOSES." FRITZ KANT, Arch. f. Psychiat. **87**:171 (May) 1929.

The author discusses the concept of the sensitive psychoses of reference described by Kretschmer and the possibilities of the superposition of an actual schizophrenic process on this form of reaction. Two cases are reported. In the first, a gradually developing tendency to paranoid interpretations and the formation of ideas of reference is analyzed, and it is shown how the evolution of it was dependent on early experiences and constitutional factors in the patient's make-up. Up to a certain stage there was no indication of definite schizophrenic symptoms, and the reaction could be considered as belonging to the group described by Kretschmer. Later in life, however, as environmental factors became particularly difficult to deal with, there was a gradual development of a paranoid schizophrenic psychosis with hallucinatory experiences and deterioration. The second case presents somewhat similar features, but with the development of an affective psychosis as a superstructure on a tendency to paranoid interpretations. The author believes that representatives of the Kretschmer reaction type are extremely rare and that in between them and the actual process psychoses (schizophrenic and affective) there are gradations more or less similar in type to the ones described in this paper. The development of these psychoses is dependent on constitutional and characterologic factors just as much as it is on whatever is causative of the process psychoses.

MALAMUD, Iowa City.

A STUDY OF MUSCLE IN CONTRACTURE: THE PERMANENT SHORTENING OF MUSCLES CAUSED BY TENOTOMY AND TETANUS TOXIN. S. W. RANSON and C. F. SAMS, J. Neurol. & Psychopath. **8**:304 (April) 1928.

Hypertonic contractures, whether developed in spastic paralyses or of reflex origin, depend on a continuous tonic innervation of the affected muscles. Myostatic contractures, such as those following tetanus, tenotomy or immobilization of a limb in a plaster cast, are due to a shortened condition of the resting muscle and are entirely independent of the nervous system. This state is maintained after section of the motor nerve or after the death of the animal. The extensibility of such a muscle is decreased, while its elasticity remains normal. No microscopic evidence explains this phenomenon.

In tetanus contracture and in that caused by tenotomy a selected group of fibers were shortened about 50 per cent of their normal length. In tetanus contracture the weight of the muscle remained normal, but after tenotomy there was loss of weight. A muscle in myostatic contracture cannot shorten as much as a normal muscle during nerve-muscle tetanus. In tenotomy preparations the rate

of relaxation was unaffected; in tetanus toxin preparations it was reduced. The height of contraction and the rate of relaxation of a muscle in tetanus contracture are the same whether the muscle is stimulated directly or through its nerve. This shows that the defective contraction cannot be explained on the basis of involvement of the nerve or nerve endings.

FAVILL, Chicago.

A NEW SIGN OF CEREBELLAR DISEASE. F. I. WERTHAM, J. Nerv. & Ment. Dis. **69**:486 (May) 1929.

Adiadokokinesis, or the inability to repeat voluntary rhythmic movements at rapid speed, has been shown in Parkinson's syndrome, Friedreich's ataxia, spastic paralysis, hemiplegia and other conditions that are not purely cerebellar. It was the object of the author's experiments to test the regularity factor alone in alternating movements, and the patient was made to tap definite rhythmic tattoos on an ebonite plate attached to a signal marker and revolving drum. Ability to cooperate, previous musical training, as well as left-handedness were taken into account. Comparisons between the affected and unaffected arms in the accuracy of rhythmic patterns were made and a characteristic disturbance was discovered consisting in loss of ability to maintain a given rhythmic pattern. This disorder was found more marked when both hands were used at the same time. The term arrhythmokinesis is given to this disturbance which does not coincide in occurrence with that of adiadokokinesis. Advanced cases of parkinsonian rigidity showed no arrhythmokinesis, whereas five cases of cerebellar involvement, verified by operation, showed the disorder definitely. The author offers the test as more specific of cerebellar dysfunction than adiadokokinesis.

HART, Greenwich, Conn.

THROMBOANGIITIS OBLITERANS. EDGAR V. ALLEN, Am. J. M. Sc. **178**:237 (Aug.) 1929.

The author considers that many reports of Raynaud's disease or erythromelalgia are in reality thrombo-angiitis obliterans and that these errors are avoidable because of the ease of proper diagnosis. This disease is defined as an inflammatory disease of the arteries and veins of the extremities with resultant occlusion. Not only may palpable arteries be involved but more peripheral ones may be affected without involvement of larger ones. Involvement of the radial or ulnar artery may be diagnosed first by compression of one or the other artery in the two hands and then comparing them for color changes on elevation, etc. The patient is first made to expel as much blood as possible from the hands by clinching them. This test is described because one artery may be involved without the other, in which case normal color reactions would be present because of the dual blood supply to the vascular tree of the hand if the other artery were not mechanically occluded. Only 50 per cent of the author's 300 patients were Jews. This is interesting because the disease is usually considered peculiar to Jews. The disease is often patchy in its distribution and thus may involve only the ulnar or radial artery, or even only one of the smaller branches.

WAGGONER, Ann Arbor.

INNERVATION OF THYMUS. L. PINES and R. MAJMAN, J. Nerv. & Ment. Dis. **69**:361 (April) 1929.

The authors, using the Cajal silver impregnation methods of staining sections of the thymus, have found nerve bundles entering the gland and ramifying between lobules, through the interstitial tissue. These nerve bundles were found escorting the vessels at a great distance, forming nerve plexuses, one type in the adventitia, the other in the tunica media. The latter plexuses contain the vasomotor nerves. They found terminal nerve apparatus of an ovoid or bulblike shape in the connective tissue between the lobules. These were considered as primitive receptive organs. The fibers are thicker than the vascular nerve fibers and do not show any varicosity. Nerve fibers were seen to penetrate into the lymphoid lobule and spread diffusely

throughout the parenchyma, with lateral branches and terminal ramifications which end with small knobs adjacent to the cells. They identify a pericorpuscular innervation in Hassel's corpuscles in which the nerve fiber surrounds the corpuscle outward or by terminal ovoid-like thickenings. Sympathetic ganglion cells in the thymus gland were not observed. The authors conclude that the thymus is well supplied with differentiated sympathetic and cerebrospinal nerves, both afferent and efferent, and that all the elements of the gland are under nerve control.

HART, Greenwich, Conn.

FAMILIAL PLANTAR PERFORATING ULCER WITH PROBABLE LUMBOSACRAL SYRINGOMYELIA IN TWO BROTHERS. G. GUILLAIN and A. THÉVENARD, Ann. de méd. **25**:267 (March) 1929.

Syringomyelia has been reported in different members of the same family, but only Bruns, Schultze and Bremer found a combination of this disease with symmetrical gangrene of the feet. To these cases the authors add the case reports of two brothers. One developed the ulcerations at the age of 13, the other at 16. In the second case scar formation after prolonged rest in bed interrupted the disease process in two intervals of three years and one year, respectively. Neurologic examination during the third period revealed exaggerated patellar reflexes, absence of plantar reflexes and normal cremasteric and abdominal reflexes. There was a bilateral zone of thermohypalgesia beginning at the middle of the calves of the legs which gradually continued into a zone of complete anesthesia around the heels. Sensibility to pain was diminished in the soles of the feet and completely abolished within the ulcerations. Tactile sensibility was not disturbed. There were no sphincter or genital disturbances. There was excessive perspiration on the lower halves of the calves of the legs and on the feet. Roentgen and spinal fluid examinations gave negative results.

WEIL, Chicago.

EPILEPTIC MANIFESTATIONS IN SCHIZOPHRENIC AND MANIC-DEPRESSIVE PSYCHOSES. J. NOTKIN, J. Nerv. & Ment. Dis. **69**:494 (May) 1929.

Krisch, Gruhle, Vorhastner, Urstein and others have described cases of dementia praecox and manic-depressive psychosis in which epileptiform seizures have occurred. Urstein found only 3.5 per cent of the patients with epileptiform attacks in a group of 2,700 patients, and other authors consider it a relatively rare phenomenon.

The author presents eight cases of his own, three manic-depressive and five schizophrenic cases, in which epileptic manifestations of major and minor types have been observed. He disagrees with the theory of Urstein that all epileptics are catatonics, and that epileptic attacks are of catatonic character, because of the typical traits of epileptic psychosis and its different type of deterioration. He finds a psychogenetic explanation of the seizure as a flight from intolerable adjustment inadequate in the midst of schizophrenic or manic reactions which are themselves regarded as established adjustments. Furthermore, no epileptiform seizures are observed in the more intolerable depressed phases. A history of head trauma, the appearance of seizures in teething periods and during pregnancy or emotional stress is noted.

HART, Greenwich, Conn.

THE CARBOHYDRATE METABOLISM IN PROGRESSIVE MUSCULAR DYSTROPHY. M. S. SCHEIMANN, Arch. f. Psychiat. **87**:665 (June) 1929.

The blood sugar was studied in eight cases of progressive muscular dystrophy to determine whether any differences could be found between the carbohydrate metabolism of these patients and that of normal persons. The blood sugar during fasting, with the patient at rest, showed no essential deviations outside of the fact that it was universally low (from 60 to 70 mg.). The blood sugar curve following administration of sugar showed a definite hyperglycemic curve along with some glycosuria. A similar condition was found on a study of the blood sugar follow-

ing muscular exertion. Both of these observations were similar to those made on diabetic patients. The author considers these results significant in that they show that while these patients exhibit no abnormal metabolism when at rest, their ability to metabolize higher quantities of sugar, or the normal quantities during muscular exertion, are seriously interfered with. He believes that this may give some leads in the study of the pathogenesis of the disease and its etiology. Further study should be undertaken, however, on both the other aspects of carbohydrate metabolism and the metabolism of other substances (proteins, fats, salts, etc.).

MALAMUD, Iowa City.

THE PROBLEM OF JUVENILE BEHAVIOUR DISORDERS IN CHRONIC EPIDEMIC ENCEPHALITIS. T. R. HILL, J. Neurol. & Psychopath. **9**:1 (July) 1928.

The clinical features of juvenile behavior disorders in chronic epidemic encephalitis are described with illustrative cases. Intelligence was preserved, and insight was clear. The conduct was compulsive and of a crude, primitive and instinctive type. It is suggested that there is an overpowering increase in the pleasure that normally comes from obeying instinctive tendencies and in the displeasure that normally comes from obstructing them. The pathologic change is of an organic nature, causing exaltation of thalamic function either by thalamic release through loss of cortical inhibition or by chronic irritation and excitation. The encephalitic virus is known to center on the thalamostriatal level, and the cortex is obviously not seriously involved. The bradyphrenia of the parkinsonian syndrome is characterized by good intelligence with a subjective state of mental inertia and loss of interest or feelings. It is contrasted with the mental state in cases with behavior disorder and may well be due to a depression of thalamic function. Hence, one may assume that the initial irritative lesion develops finally into a destructive one.

FAVILL, Chicago.

SOMATICALLY CONDITIONED ANXIETY DREAMS. E. EICHENBERGER, Arch. f. Psychiat. **87**:640 (June) 1929.

Some emotional states have been shown to bear definite relationship to somatic diseases. The most frequently encountered instance is that of the anxiety states in cases of heart disease. The author discusses the general concept of anxiety (Angst) and its relationship to fear. The difference between the two consists in the fact that fear presupposes an object, whereas in anxiety no special stimulating object is necessary. In dreams, in which vague emotional states are occasionally transposed into definite experiences, anxiety states may be experienced as definite fears. The dream material the author presents demonstrates this fact nicely.

Nineteen patients with different forms of cardiac disease were utilized in this study. The physical condition was followed regularly, special attention being paid to the kidney elimination. At the same time, the patients were instructed to tell the examiner whatever dreams they had. It was found that decompensation of the cardiorenal apparatus was generally preceded by marked anxiety dreams. These were almost invariably followed by a drop in the urinary output. In cases in which the latter fluctuated, the dreams occurred regularly before the drop took place. The author does not attempt to analyze the different dreams, although the subject matter offers some interesting data for symbolic interpretation.

MALAMUD, Iowa City.

BRAIN TUMORS IN CHILDHOOD: A CLINICOPATHOLOGIC STUDY. FREDERIC H. LEAVITT, Am. J. M. Sc. **178**:229 (Aug.) 1929.

In contrast to the older current belief the author considers that brain tumors occur fairly frequently in early life, the ratio with the adult being about 1:14, a large percentage of the cases in early life being cerebellar (60 per cent) medulloblastomas. The symptomatology usually begins with a rapid onset of vomiting and headache, followed by drowsiness and choked disk, occasionally with enlargement

of the head. In addition are the usual motor signs which are of localizing value. The three most frequent types of tumors are the tuberculomas, the congenital tumors (which are said to be most often suprasellar), and the glioma group which are most often cerebellar and usually arise from the roof of the fourth ventricle and extend into the vermis of the cerebellum. In this situation cerebrospinal fluid block occurs early with its concomitant symptomatology. The author believes that symptoms pointing to the presence of a cerebral neoplasm should be recognized earlier and thus allow proper treatment to be started earlier.

WAGGONER, Ann Arbor.

THE ARNETH BLOOD-COUNT IN IDIOCY AND LOW-GRADE IMBECILITY, WITH SPECIAL REFERENCE TO THE INCIDENCE OF TUBERCULOSIS AND TUBERCULAR INFECTIONS. STANLEY R. TATTERSALL and CYRIL J. THOMAS, J. Ment. Sc. **75**:64 (Jan.) 1929.

The number of nuclear lobes in 100 polymorphonuclear leukocytes of the blood (the Arneth count) is very low in idiots and imbeciles as compared with that in normal persons and low as compared with that in psychotic patients. Of 142 feebleminded persons studied the average for males were: imbeciles 192 and idiots, 177; for females: 195 and 181, respectively. The figures therefore appear to be lower for the more defective types and slightly higher for females than for males. The authors, who regard this count as in some way an "index of vitality," consider the reversal of the usual higher index in males than females as the result of the observed better physique in the females of this series. The principal value of a low count, however, is as an index of some infective process, especially of tuberculosis. Clinical arrest of a tuberculous process is in all cases accompanied or preceded by a rise in the count.

SINGER, Chicago.

A CASE OF MYASTHENIA GRAVIS. ARIE QUERIDO, J. Nerv. & Ment. Dis. **69**:522 (May) 1929.

The case of a woman aged 36 is presented with all the clinical manifestations of myasthenia gravis, with increased fatigability, diplopia, dyspnea, low blood pressure and Jolly's myasthenic reaction of degeneration. She died in an asthmatic attack. Autopsy showed pallor of muscles, and microscopic examination showed increase in the nuclei of the cardiac muscle with some fragmentation of fibers. Perivascular foci containing leukocytes, lymphocytes, plasma cells and fibroplastic tissue were common in the striated muscle, liver, lung and kidney. The walls of vessels running through such foci were infiltrated with the same type of cells. Supported by some evidence from the literature, the hypothesis is offered that myasthenia gravis is a general vascular disease to be defined pathologically as a perivasculitis chronica proliferans. In the author's opinion the loss of muscle strength is only one symptom of this general disease of the small vessels.

HART, Greenwich, Conn.

NEUROLOGIC ASPECTS OF POLYCYTHEMIA VERA. THOMAS WILLIAM BROCKBANK, Am. J. M. Sc. **178**:209 (Aug.) 1929.

Patients suffering with polycythemia vera often have neurologic symptoms which may confuse the clinical picture. More particularly are they apt to simulate brain tumor. It is frequently associated with headache or migraine. In a study of 56 cases, 33 patients had headache, 30 had vertigo, 15 had general weakness and other neurologic symptoms were present in lesser numbers. Objective neurologic signs were noted only in those cases with vascular accidents which are said to occur fairly frequently in this condition. Thus it was considered that the neurologic aspects of polycythemia vera are extensive and sometimes confusing as to symptoms. The disease itself shows little of primary neurologic interest except in those cases with vascular accidents. The diseases associated with polycythemia vera are varied and are often neurologic in nature.

WAGGONER, Ann Arbor.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Regular Meeting, Feb. 21, 1929

HARRY C. SOLOMON, M.D., *President*

A CASE OF FACIAL SPASM (TIC CONVULSIVE) TREATED WITH TRICHLORETHYLENE. DR. JACQUES DE BUSSCHER, read by DR. JAMES B. AYER.

Mrs. B. N. H., aged 49, had complained of progressive paroxysms of facial spasm of the left side during the past five years. The attacks began with infrequent twitchings of the orbicularis oculi muscle; after a year, the whole left side of the face was involved in the spasm, although most marked in the orbicularis oculi. Recently, the attacks had also involved the platysma. The attacks came at any time but were especially severe toward night. There had never been any pain connected with them.

Physical and neurologic examination gave negative results with the exception of the paroxysmal facial spasm. Laboratory examinations also gave negative results. There was no evidence of focal irritation of the facial nerve. There was no collateral evidence suggesting a psychogenic cause for the attacks.

On the theory that the attacks might be diminished by working on the sensory reflex arc, trichlorethylene, 20 drops three times a day, was administered. There was almost immediate objective and subjective improvement following its administration. The patient was followed up for six months, during which time the spasms were controlled with this drug; but when the doses were stopped, the paroxysms gradually returned, although a little more slowly after each administration.

At this time the patient was told to stop treatment. She was seen again five months after the use of trichlorethylene was discontinued. Occasional slow contractions of the orbicularis oculi alone remained as evidence of her original difficulty.

Two other patients were given trichlorethylene, with immediate improvement in symptoms, but it has been impossible to follow them. Dr. W. J. Mixter told the author that he had seen improvement in another patient treated similarly by him.

DISCUSSION

DR. MABEL ORDWAY: Would there have been any harm in continuing the use of trichlorethylene for any length of time in order to prevent recurrence? When one gave bromide it was always given for two years after the patient's last attack.

DR. K. M. BOWMAN: Were any of the cases bilateral?

DR. J. B. AYER: All the cases were unilateral. I consider that this patient was undertreated rather than overtreated. We now use trichlorethylene which is the same thing, five times daily, between 20 and 30 drops a dose. We have seen no alarming symptoms from this régime. There is apparently no tendency to habit formation. I repeat that I am reticent about reporting this single case; but as we have had others which have also improved, it would seem as if trichlorethylene therapy in tic convulsive were a logical procedure.

INIENCEPHALY. REPORT OF A CASE. DR. B. H. APPEL and DR. J. KASANIN.

Iniencephaly is a developmental condition characterized by the presence of an imperfect formation of the occiput in the region of the foramen magnum. The condition is extremely rare. It was first described in 1836 by St. Hilaire, who reported three cases. The subject received no further attention until 1897, when

Davis reviewed twenty-five cases which he collected from literature. In 1904, Ballantyne reported seven additional cases. In 1905, Dorland reported a case and mentioned the presence of two additional cases in the museum of the University of Chicago. The last mention of the subject was by Welz and Lieberman, who reported a case in 1927. The extreme rarity of the condition is apparent in the relatively small total of thirty-nine cases which have been reported to date.

The cardinal signs of iniencephaly are: Incomplete formation of the foramen magnum; retroflexion of the head, and spina bifida, which, however, may not be present in all cases.

A child, aged 5 weeks, was brought into the office of Dr. B. Appel on account of retraction of the head. The parents were Italian, both in good health. The

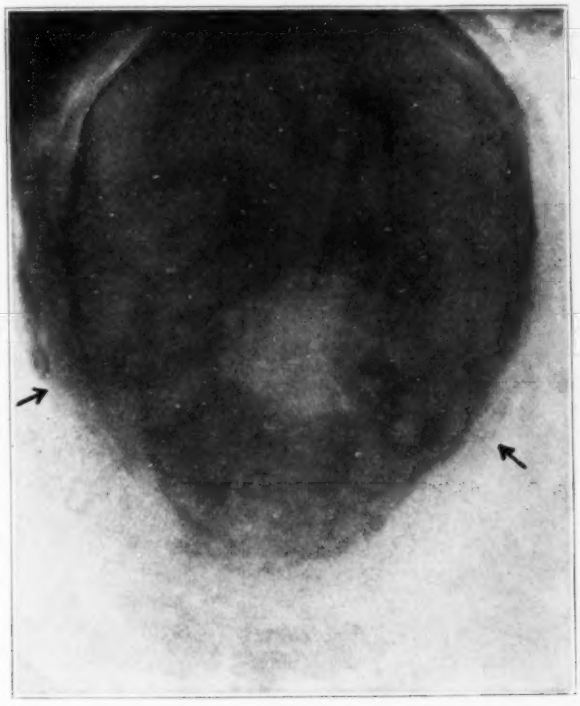


Fig. 1.—Roentgenogram, showing enlargement of the foramen magnum in child 5 weeks old.

family history was negative for nervous and mental diseases. The patient was the second child, the older child being normal. The history of birth was normal with the exception of marked cyanosis at birth. The baby was breast fed and was gaining well. The mother noticed that the baby had had a retracted head since birth but that she was able to bend the child's head anteriorly without difficulty.

Physical examination gave negative results. The patient was a well developed and well nourished white infant. There was marked retraction of the head backward so that the chin pointed upward. The head and trunk made an angle of 145 degrees. When the infant was placed on the abdomen it retracted the head backward. The head could be flexed so that the chin touched the manubrium sterni but as soon as the pressure was released, the head tilted backward. There were no other stigmas, with the exception that the shape of the head was some-

what oxycephalic and had a tendency toward mongoloid features, with broad cheek bones and slanting eyes. The pupils reacted well to light. Examination of the fundi revealed clear margins of both optic disks. No cherry red spots were observed. The cranial nerves were normal with the exception of a slight facial asymmetry, with perhaps a slight flattening of the left side of the face. There were no spasticities or palsies. The tendon reflexes were present. There was a bilateral Babinski sign, as one would expect in an infant. The lower extremities showed no evidence of spastic or flaccid paralysis. The roentgenograms of the cranium and spine showed an incomplete formation of the foramen magnum. There was no evidence of deviation from the normal in the cervical or the dorsal spine.

The case was reported in full in the *New England Journal of Medicine and Surgery* (**200**:1295 [June] 1929).

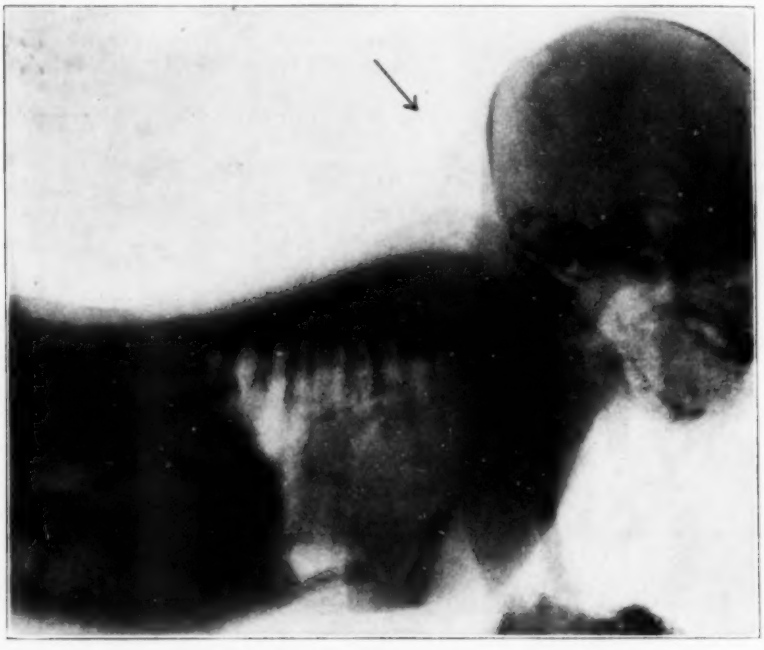


Fig. 2.—Roentgenogram, showing marked retroflexion of the head in the same patient as in figure 1.

PHILADELPHIA NEUROLOGICAL SOCIETY

Regular Meeting, May 24, 1929

CLARENCE A. PATTEN, M.D., *President, in the Chair*

CASE OF SPINAL CORD TUMOR WITH CALCIFICATION OF THE CHOROID PLEXUS. DR. FRANCIS C. GRANT.

Clinical History.—E. K., aged 42, a white woman, was referred to the Neurosurgical Clinic of the Graduate Hospital by Dr. T. H. Weisenburg, with the chief complaint of numbness in legs. Two years before entrance, a fall was followed by intense pain in the back, in the sacral region, for two or three days, and soreness for a month. One year later, following a year of perfect health, she

noted numbness in the toes of both feet; the toes felt as if asleep. Gradually the numbness ascended, involving both legs up to the waist line. No motor weakness of any description was noted at this time. For seven or eight months there had been a staggering gait. Her children complained that she walked as though drunk. Two months before entrance there occurred the onset of weakness in both legs. She went to bed one month before examination being unable to walk at all. There had been no sphincteric involvement. Three months before entrance into the clinic, a sticking pain began in the right side of the head. There had been a ringing in both ears and an onset of deafness. Headache began at this time; there had been no vomiting.

Neurologic Examination.—The optic nerve heads were pale but not atrophic. There was noted a weakness of the left internal rectus. The visual fields were full. Horizontal nystagmus, both to the left and right, was present. There was some anesthesia in the second division of right fifth nerve, and marked bilateral diminution of hearing was present. The upper extremities were normal and there was no ataxia. Both legs of the patient were weak in all movements, especially the right leg. The peripheral portions of both legs were weaker than the upper portions. The patient was able to walk fairly well but staggered definitely to the right. The gait had a wide base but was not spastic. The right leg was weaker than the left in walking.

Reflexes: There was diminution of the left corneal reflex; the biceps and triceps jerks were normal; the abdominal reflexes were lost; the patellar jerk was hyperactive equally on both sides; the achilles reflexes were lost bilaterally; and there was a bilateral Babinski sign.

Sensory Examination: There was impairment of all forms of sensation up to the level of the sixth and seventh thoracic dermatomeres. Impairment of the sense of position in the toes was noted. Vibratory sense was impaired as far as the pelvis.

Laboratory Studies: The examination of blood showed a moderate anemia. The urine was normal. Serologic tests were negative. The cell count of the spinal fluid was 2, the colloidal gold test, negative. Gastric analysis gave a low acidity.

Bárány Test: There was complete loss of function in all canals of both ears, with good hearing. This suggested a degenerative process involving both sides of the medulla.

Diagnosis was: Anemic cord changes, myelitis or multiple sclerosis and cord tumor had to be considered. Optic atrophy, with loss of the abdominal reflexes and the diffuse nature of the lesions suggested multiple sclerosis. A definite sensory level with motor loss suggested a myelitis or tumor. If it was a tumor, it was curious that no sphincteric involvement had occurred. Anemia and low gastric acidity brought up the question of anemic cord changes.

Roentgenogram Studies.—Bilateral calcified areas, symmetrically placed in the middle of the right and left cerebral lobes, were present. The spine showed osteo-arthritis and spina bifida occulta.

Spinal Fluid.—To determine the presence of block, a lumbar puncture with the Queckenstedt test was done. This suggested an incomplete block but the test was inconclusive. The fluid was clear and colorless; the presence was 6 mm. of mercury. The sensory and motor symptoms became more pronounced after the lumbar puncture. Combined lumbar and cistern puncture gave evidence of a complete block. There was a free rise in the cistern manometer but none in the lumbar following jugular compression. This test seemed to verify a diagnosis of tumor.

Since we were uncertain as to the significance of calcification in the cerebral hemispheres, although from the position it seemed likely that the calcification lay in the choroid plexus, it was decided to attack the cord lesion first. Any cranial lesions were probably inoperable.

Diagnosis.—The working diagnosis was a cord tumor at the level of fifth thoracic and sixth thoracic segments.

Operation.—A laminectomy to expose the cord from the level of the third to the eighth thoracic segments, was performed, the second to the sixth laminae being removed. A tumor was found lying posterolaterally to the cord on the left in the lower end of the wound, involving the seventh and eighth thoracic segments. The tumor was intradural but extramedullary and was encapsulated. The dural attachment was removed. The tumor contained a plaque of bone.

Postoperative Course.—The patient walked out of the hospital, using a cane, ten weeks after removal of the tumor.

Comment.—Points of interest are: 1. The history of pain in the back following a fall; 2. numbness as the first symptom—the patient never had pain; 3. bilaterality of the symptoms—both legs were simultaneously involved; 4. the lack of the sphincteric involvement—this is rare in tumor; 5. the symptoms suggestive of other conditions, such as anemic cord changes and multiple sclerosis; 6. the symptoms were made worse by lumbar puncture which suggested a tumor, the position of which was changed by the removal of fluid; 7. the importance of combined puncture to demonstrate a block in obscure cases; 8. the calcified lesions in the cerebral hemisphere which might account for the nystagmus, loss of hearing, abnormal Bárány reactions and staggering gait—the lesions probably were in the temporal lobe; 9. the type of tumor found, containing a calcified plaque which suggested a pathologic reaction of the same type as that seen in the roentgenogram of the cerebrum; 10. the prompt postoperative recovery following removal of the tumor.

ALTERNATING OCULAR SYMPATHETIC PARESIS IN A CASE OF CHRONIC ENCEPHALITIS. DR. W. B. CADWALADER and DR. W. E. FRY (by invitation).

This patient was presented because of the interesting type of pupillary reaction which he showed to cocaine. He was studied in the medical wards of the University Hospital and a diagnosis was made of chronic encephalitis. When first seen, he was thought to have a left-sided Horner's syndrome. Further observation brought out the fact that the pupils varied from time to time; at one time the right pupil would be smaller and at another the left. When a 2 per cent solution of cocaine was instilled in each eye, whichever pupil was smaller at the time of the instillation failed to dilate as well as the other. This test was done four times, twice when the right, and twice when the left pupil was the smaller.

The following measurements were taken: (1) With the right pupil smaller. On January 4, the right pupil measured 3 mm. and the left, 4 mm. The right fissure was 10.5 mm. and the left, 9.5 mm. The Hertle exophthalmometer measurements were 14.5 mm. on the right, and 15 mm. on the left. Thirty minutes after 2 per cent cocaine was instilled, the measurements were: right pupil, 4 mm. and left, 7 mm. Each palpebral fissure became 12 mm. The right pupil had changed from 3 to 4 mm. and the left from 4 to 7 mm. (2) With the left pupil smaller. On January 6, the right pupil measured, 4 and the left pupil, 3 mm. Thirty minutes after the instillation of cocaine the right pupil measured, 4.5 and the left, 3 mm.; sixty minutes after the instillation, the measurements were 6 on the right and 5 mm. on the left. (3) With the left pupil smaller. On January 8, the right pupil measured, 3.5 and the left, 2.5 mm. Sixty minutes after the instillation of cocaine the right pupil measured, 5 and the left, 3.5 mm. (4) With the right pupil smaller. On January 9, the right pupil measured, 3 and the left, 4 mm. Sixty minutes after the instillation of cocaine the right pupil measured, 3 and the left, 5.5 mm.

Examination of the fundus gave negative results except for some slight pallor of the temporal side of the disks. The visual fields were concentrically contracted. Roentgen examination of the chest gave negative results, and there was no evidence of the presence of cervical ribs.

From these tests and accepting the cocaine test as indicative of ocular sympathetic interference, we believe that this is a case presenting an alternating type of intra-ocular sympathetic paresis.

DISCUSSION

DR. CADWALADER: In 1920, I reported to this society (*J. A. M. A.* **47**:1315 [May 8] 1920) the occurrence of bilateral sympathetic ophthalmoplegia in a case of epidemic encephalitis. The necropsy showed the characteristic inflammatory lesions in the medulla oblongata, as well as in other portions of the midbrain. The sympathetic ocular phenomena were attributed to implication of the sympathetic fibers in their course within the dorsomedial portions of the medulla oblongata. This observation was received with some skepticism, because of the fact that the reaction of the pupils had not been tested with cocaine. Dr. Fry has proved that in his case of epidemic encephalitis the sympathetic ocular fibers of each side were affected, because they did not react properly after the instillation of cocaine.

Dr. Spiller observed in his cases, reported before this Society under the title of "Subcortical Epilepsy," that unilateral sympathetic ophthalmoplegia can be produced by a lesion in the subthalamic region.

So far as I know, no other cases of bilateral sympathetic ophthalmoplegia have been observed from lesions of the brain stem.

DR. WINKELMAN: I would not agree with Dr. Cadwalader's interpretation of the cause of enlarged palpebral fissures in lenticular cases. No one, as far as I know, has traced the sympathetic fibers into the lenticular nucleus. My own explanation would be that the lid muscles partake of the same rigidity that characterizes the rest of the musculature and in that manner produces a moderate retraction of the lids.

A CASE OF SECTION OF THE TRIGEMINAL AND GLOSSOPHARYNGEAL NERVES THROUGH THE POSTERIOR FOSSA (DANDY METHOD). DR. NICHOLAS GOTTEN.

This case is presented to illustrate the facial pain remaining after removal of the trigeminal, facial and glossopharyngeal nerves. The procedure was undertaken by the Dandy method of approach through the posterior fossa, because of the situation of a malignant growth which prevented the usual Spiller-Frazier operation.

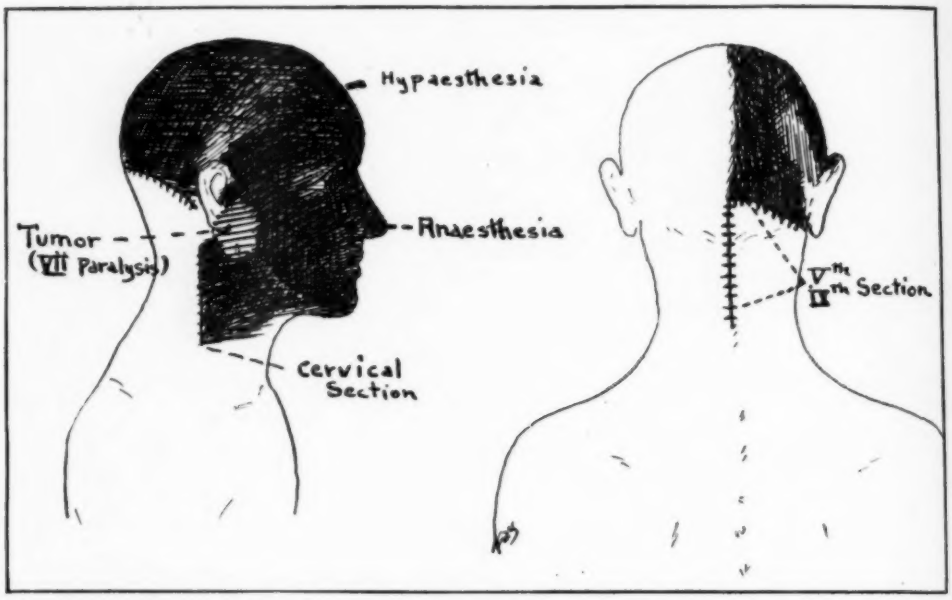
Mrs. C. D., aged 61, first noticed a small movable nodule in the right parotid region, in November, 1928. In the course of a few weeks, as the nodule became larger, she experienced pain in the region of the jaw and across the maxilla. In December, the greater portion of the nodule was removed at the New York Post-Graduate Hospital. The histologic diagnosis at this time was chronic inflammation with endothelial proliferation.

Immediately following the operation, the patient had a complete paralysis of the seventh nerve on the right side. The wound healed and the patient was relieved until January, 1929, when she had a recurrence of the pain in the right side of the face. She was then referred to Dr. J. B. Carnett, of Philadelphia, who advised roentgen and radium therapy. She received two courses of roentgen and radium therapy, but in April, 1929, the pain had become so severe that she was unable to continue treatment. She was using approximately 1 grain of morphine daily for control of the pain. The pain at this time was distributed chiefly to the second and third divisions of the fifth nerve and was continuous in character. She was referred to Dr. Temple Fay for section of the fifth nerve which was done May 7, 1929, according to the technic of Dandy, as follows:

A unilateral suboccipital craniectomy was performed on the right side, the incisions extending in the midline from the external occipital protuberance to the sixth cervical vertebra, and along the occipital ridge to the tip of the mastoid process. The muscle was freed from the occipital bone. The bone was rongeured from the midline to the mastoid process, followed by dissection of the muscles down to the foramen magnum. An approach was then made to the right cerebellopontile angle, and the seventh and eighth nerves were encountered. The ninth, tenth and eleventh nerves were also seen. The fifth nerve could be seen at the apex of the triangle. The root of the trigeminus was approached, and a hook was inserted around it. The root of the fifth nerve was avulsed.

It was interesting to note that the posterior portion of the root separated from the anterior portion, so that the fibers supplying the eye and approximately the first division were not entirely involved in the avulsion. The motor root was also saved. After carefully inspecting the area of avulsion, attention was then turned to the ninth and tenth roots, the ninth being sectioned, and the upper two branches of the tenth, thought to be sensory, were also avulsed. The wound was then carefully inspected for bleeding. Some slight, superficial cortical bleeding was controlled by a muscle graft, and complete hemostasis was obtained. The dura was closed with silk; the muscles were reconstructed over the decompressed area, and a careful water-tight closure was made, not only in the muscle bed, but in the subcutaneous and skin levels as well.

The patient made an uneventful recovery, and was completely free from pain within the distribution of the fifth cranial nerve. She required no sedatives and gained in weight. She had a dull aching pain along the vascular distribution to the neck and face. The vessels were tender to deep pressure.



Second and third divisions, with marked impairment in the first division of cranial nerve divisions in patient, following operation.

Following operation, the sensation for pin point as well as tactile sense was lost in the second and third divisions, with marked impairment in the first division (see illustration). The corneal reflex was present. It was evident that sectioning the posterior root through the Dandy approach produced the same anesthesia as in the Spiller-Frazier operation. The selective loss of pain sense was not demonstrable in this case. As the ninth nerve was also sectioned at the time of the operation, the residual pain distributed along the course of the carotid artery, temporal artery, the infra-orbital and the supra-orbital strongly suggested the presence of another underlying pain mechanism, not associated with the fifth or ninth nerves. As the seventh nerve was entirely paralyzed in this case, one can assume that the fifth, seventh and ninth nerves were inactive and the pain distribution represents vascular pain fibers carried probably through the vagus.

This is further suggested by the fact that the upper cervical plexus branches were sectioned later so as to produce sufficient cervical anesthesia to rule out these fibers as being responsible for the vascular tenderness remaining.

DISCUSSION

DR. TEMPLE FAY: This patient is 61 years of age, and it is two weeks since the operation. She was confined to her bed for some weeks prior to the operation, and has improved a great deal. She presents for the first time, as far as I can determine, a condition which calls for section of the fifth, seventh and ninth cranial nerves. The seventh had already been removed; I sectioned the ninth and fifth. Therefore, there cannot be any sensory nerve supply to carry sensation deep in that area unless it be the vagus. The patient is anesthetic to pain, heat, cold and deep pressure about the face on the right side; as far as we can determine by tests applied to the skin surface, she is anesthetic in this area. If, however, one pinches the skin or deeply presses on the arteries — facial, temporal or occipital — one will produce pain. Therefore, the question comes up as to where does this vascular pain now enter the nervous system to reach consciousness? It does not enter by the fifth, seventh or ninth nerves in this case. From other cases I have shown, it is known that it does not enter by way of the cervical sympathetic trunk or the superficial cervical branches. I strongly suspect that the vagus carries these vascular fibers of pain.

DR. FRANCIS C. GRANT: I am interested to hear that Dr. Fay could not demonstrate that the sense of touch remains after avulsion of the sensory root of the fifth nerve in the posterior fossa. I have carried through this posterior avulsion of the sensory root on three occasions and in none of them could retention of touch be demonstrated. Dandy claims, following the removal of the sensory root of the fifth cranial nerve close to the brain stem by the suboccipital approach, that sense of touch is often unimpaired while the sense of pain is lost. He puts this forward as one of the principal reasons for avoiding the use of the posterior approach, rather than the route through the middle fossa.

If it were true that section of the sensory root from behind did spare the sense of touch over the face while removing pain, this only would probably justify the much more difficult technical procedure of avulsing the root by the route Dandy suggests. I have not found this to be the case in the patients on whom I practiced it. Both touch and pain were lost, and furthermore, one patient developed an interstitial keratitis. As the posterior approach is so much more difficult in technic than the temporal route, and as the patients postoperatively may show evidence of cerebellar involvement for a short time, I certainly do not feel justified in changing the satisfactory technic which has been developed by Dr. Frazier for subtotal avulsion of the sensory route of the fifth cranial nerve. By subtotal avulsion the pain is relieved, the area of numbness in the face is reduced to a minimum, and interstitial keratitis never occurs.

TWO INSTANCES OF OPHTHALMIC VASCULAR DISEASE; ONE WITH VISUAL, THE OTHER WITH MOTOR IMPAIRMENT. DR. ROSS H. THOMPSON.

Case 1 is of interest largely because of the rather rapid and complete recovery of an acute ophthalmoplegia.

CASE 1.—A fairly active man, 71 years of age, during September, 1929, suddenly developed a lateral diplopia, which was soon followed by ptosis of the left eyelid and pain in the left supra-orbital and temporal regions. He was seen at the Orthopaedic Hospital and Infirmary for Nervous Diseases in the service of Dr. Weisenburg four weeks after the onset. At that time, there was no diplopia, but the ptosis was almost complete and ocular movements on the left side were markedly impaired in all directions. The pupils were equal and reacted to light and in accommodation. Later, the left pupil was noted to be dilated. The eye-grounds showed the usual signs of arteriosclerosis, but they were not marked; there were no scotomas or restrictions of the visual fields, and acuity of vision was a little better in the affected eye than in the other, though it was impaired in both. There was no objective disturbance in the area of the fifth cranial nerve. Wassermann tests of the blood and spinal fluid were negative; the blood pressure was systolic and 110 diastolic; roentgen examinations showed no involvement of the sinuses and the sella appeared normal.

Gradually, within twelve weeks, all the extra-ocular movements became normal in range excepting a slight impairment of external rotation. The pupillary sphincter still showed some weakness as indicated by the dilated left pupil. Pain had subsided.

Because of the suddenness of the onset and the rapid clearing of symptoms in a man of his age with hypertension, a vascular lesion was thought of either back of the orbit or within it. In looking over the anatomy of the parts two likely locations were noted. Just behind the orbit and the sphenoidal fissure the internal carotid artery, before it terminates in the anterior and middle cerebral arteries, is surrounded by the cavernous sinus and closely associated with the third, fourth and sixth cranial nerves and with the ophthalmic division of the fifth. An aneurysm here, causing pressure on these nerves, was thought of, but the weakness in this diagnosis is the lack of evidence of pressure on the optic nerve with corresponding restriction in the visual field of the left eye. Nevertheless, Veits reported just such an instance from the Cushing clinic (*J. Nerv. & Ment. Dis.* **47**:249, 1918). An aneurysm of the internal carotid artery at this location was seen at operation. It was the size of a walnut and caused pressure symptoms on the third, fourth and sixth nerves and also the ophthalmic division of the fifth. The symptoms of ophthalmoplegia, however, persisted without change during the entire period of observation, which was seven months.

A second possible diagnosis was also considered, occlusion by thrombosis, atheromatous arteritis or angiospasm of the ophthalmic artery at a point distal from the giving off of the central artery of the retina. According to the most recent edition of Gray's anatomy, the central artery of the retina is the first, the most constant and one of the smallest of the branches of the ophthalmic. It is given off while the ophthalmic artery lies in the optic canal beneath the optic nerve. At about 1.25 cm. behind the bulb, it pierces the inferior surface of the coverings of the optic nerve, crosses the intervaginal space (corresponding to the subarachnoid space and enters the optic nerve, travelling in that nerve to the disk where it is distributed to the retina. This artery has no anastomosis, at least, none has ever been proved, so that a complete occlusion would result in blindness within a short time. Obviously, in this case, wherever the lesion, the central artery of the retina was not involved. If the ophthalmic artery, however, were occluded just beyond the origin of the central artery and the muscular branches involved, an ophthalmoplegia external and internal would be expected. As anastomoses are free between the muscular branches and those from contiguous branches of the internal maxillary artery, i. e., the middle meningeal, infra-orbital etc., restoration of function of the various muscles would be accounted for.

Case 2.—This patient presents a lesion, evidently in the same locality as was first considered in the previous instance, but of a different type and followed by an entirely different train of symptoms. The case is also from the service of Dr. Weisenburg at the Orthopaedic Hospital and Infirmary for Nervous Diseases. The patient had an acute hemiplegia and hemianesthesia of the right side with aphasia and with optic atrophy and blindness of the opposite eye.

In July, 1928, operation was performed for purulent appendicitis. On the tenth day, while confined to bed, the patient developed rather gradually, apparently without loss of consciousness, weakness of the right side of the face and body. There was also blindness in the left eye and aphasia. The definite order of sequence of the symptoms is not known, but, as well as an almost complete motor aphasia will permit, he apparently wished to convey the impression that the right side of the face and speech were first affected and the right extremities shortly after. Exactly when the blindness became complete could not be determined for the same reason, but when asked if he noticed it at the beginning of the other symptoms, he indicated as well as he could that he did.

He had an aphasia of the motor type, a right spastic hemiplegia, impairment of sensation for touch, pain and temperature on the right side of the head and body, and an optic atrophy and blindness in the left eye. A Wassermann reaction of the blood was negative.

It would appear that, during an attack of purulent appendicitis, an embolus must have lodged in the left middle cerebral artery. As this artery supplies the basal

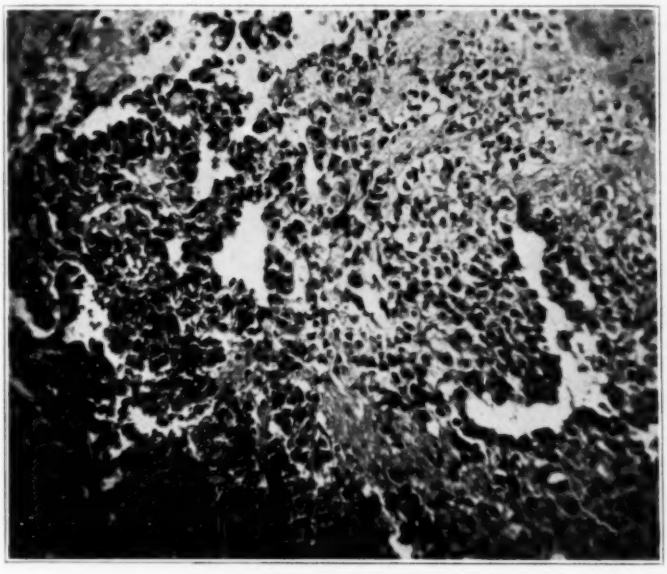
ganglia and internal capsule, the hemiplegia and hemianesthesia of the opposite side and the asphasia can readily be accounted for. Just before the termination of the internal carotid artery into its terminal branches, the anterior and middle cerebrals, it gives off the ophthalmic. Involvement of this artery, which has for one of its branches the central artery of the retina, would account for the ipsolateral blindness. Whether or not there occurred ophthalmoplegia, which cleared as in the preceding case, it is impossible to state. Certainly, no ophthalmoplegia was present, and the man had no recollection of it ever having been present.

A Report of Ten Cases of Brain Tumor with Sudden Onset of Symptoms and Review of Similar Reports. Dr. C. W. Irish.

This paper will appear in full in a later issue of Archives of Neurology and Psychiatry.

A Case of Metastatic Tumor of the Brain, Following Removal of a Carcinoma of the Testicle. Dr. William L. Long.

This case is presented because of the suddenness of onset, the violence of symptoms, the finding of a large metastatic tumor in the right lung, and because



Adenocarcinoma of the testicle.

sections are available from the original tumor which was removed twenty months before (see illustration).

The patient was a white man, aged 29, who was admitted to Dr. D. J. McCarthy's service at St. Agnes Hospital, with a chief complaint of blurred vision and headache: The day of admission was the twelfth day of his illness. On the first day of the illness, he awoke with "blurred vision" and a severe headache, which continued until the time of death, eighteen days later. The headache was frontal and worse on movement. There was no diplopia. Four days later, he coughed up several clots of blood. He had vomited three times and had had some epistaxis. The temperature had been normal or slightly subnormal.

Physical Examination.—The positive observations on the fifteenth day, were as follows: a flat note in the right upper part of the chest, anteriorly and posteriorly;

blood pressure, 112 systolic and 68 diastolic; absence of right testis; an acute inflammatory process in the left nostril, and diseased tonsils.

Neurologic Examination (Dr. Spiller).—On the sixteenth day, the pulse rate was from 54 to 64 and temperature, 98 F. All reflexes were a little more prompt than normal, and there was a slight weakness of the left side of the face. The nasolabial fold not quite so deep on the left, but not distinctly abnormal. In drawing up the corners of the mouth separately, he required a little more enforcement of the left corner to keep it drawn upward. The patient had a right homonymous hemianopia with some blurring of the optic disk. There were no signs that were positive for the left frontal lobe, left motor area, left temporal lobe or the sensory portion of the left parietal lobe. These negative observations would suggest the possibility that the lesion causing the right homonymous hemianopia was in the left occipital lobe. This was a diagnosis by exclusion and not entirely satisfactory.

On the sixteenth day, the patient got out of bed, broke a glass, and upset furniture because, he said, his headache was so violent that he could not endure the pain of it. Later in the day, he had five violent convulsions within a few hours. He did not regain consciousness after the last convulsion, and died three hours later of respiratory failure.

Laboratory Observations.—The spinal fluid showed a pressure of 8 mm., and was clear and colorless; the Wassermann test was negative, and the white blood cell count, 17,500. Roentgen examination of the chest showed the right side to have a large circumscribed mass in the right upper lobe; there were some small nodules in the right lung, which were rather indefinite.

THIRTEENTH INTERNATIONAL PHYSIOLOGICAL CONGRESS

Boston, Aug. 19, 1929

Approximately 575 papers or demonstrations were presented at the Thirteenth International Physiological Congress. Among these papers were numerous presentations of interest to neurologists and psychiatrists. A very brief outline of some of the more interesting of these communications follows:

THE ELECTRICAL RESPONSE IN SMALL GROUPS OF MUSCLE FIBERS. E. D. ADRIAN, Cambridge, Mass., and D. W. BRONK, Philadelphia.

Concentric needles lead from a restricted group of muscle fibers to the input of a three valve amplifier. The amplified action potentials are transformed into sound waves by means of a second power amplifier, and loud speaker. It is thus possible to follow by ear the frequency of the impulse discharge during a voluntary contraction.

THE VISCERAL NERVOUS SYSTEM AS A REGULATOR OF TISSUE METABOLISM. DANIEL ALPERN, Kharkow.

From his experiments on the functions of the visceral nervous system, the author concluded that the sympathetic nervous system controls the metabolism of glandular tissues, regulating their salts and nitrogen products. It controls cell permeability, and regulates the metabolism, not only by its effects on blood-vessel walls, but chiefly by control of chemical constituents and cell permeability. In unilateral disturbances of the visceral innervation (such as in syringomyelia), chemical determinations showed alterations of the blood in the affected area from that in the nonaffected area.

ON THE CONDITIONED REFLEXES AFTER AN ENGRAFTING OF THE SEX GLANDS TO DOGS. B. M. ARCHANGELSKY, Dnepropetrovsk, Ukraine.

Some homotransplantations of sex glands were made in dogs and their effects on conditioned reflexes were studied. It was found that implantation of testes essentially disturbed the equilibrium between the excitatory and inhibitory cerebral processes. The positive conditioned reflexes acquired an extraordinary stability, they were extinguished with difficulty and reestablished spontaneously in a few minutes. Formation of new positive reflexes was accelerated, but new negative conditioned reflexes were almost impossible to establish. Internal inhibition grew weak. These effects developed slowly after operation and disappeared with the absorption of the graft.

Some ovarian implantations in bitches had no effect on the cerebral activity.

Total castration breaks up the exactitude of both excitatory and inhibitory processes.

He concluded that the mechanism of the hormonal action of the male sex gland on activity of the brain is to weaken the internal inhibition and augment the excitatory process.

ON THE CONDUCTION TIME OF THE NERVOUS IMPULSES THROUGH THE CENTRAL NERVOUS SYSTEM. J. BERITOFF, Tiflis.

The afferent nerve or skin of a limb was stimulated and the action current of muscle was studied with a string galvanometer. The rhythm of stimulation of the afferent nerve was transferred through the spinal cord to the muscles of the stimulated limb in ipsilateral flexor reflexes.

The minimal latent period of the electrical responses of the muscles corresponded very often to the length of the nervous path from the stimulated nerve to the spinal cord, and back to the muscle. The rate of conduction of nervous impulses was considered to be equal to from 70 to 80 meters per second and the latent period of the electrical response of the muscle stimulated indirectly to be equal to 0.0015 second.

The rhythm after strychnine poison was studied, and it was found that the excitatory processes were also transmitted without delay from one symmetrical half of the cord to the other. Also, that through the whole nervous system, and in certain cases the cerebrum itself, the same was true. The time of conduction, after stimulation of the cortex was found to correspond exactly to the length of the nervous path in certain conditions and in others it was longer by 1-2 sigma before and after strychnine poisoning.

He suggests, on the basis of his experiments, that the passage of the excitatory processes from the excited to the nonexcited part depends on the stimulating action of electrical effects of the excited part on the nonexcited part.

AN INFLUENCE OF SYMPATHETIC NERVES ON MUSCLE GLYCOGEN. S. W. BRITTON, University of Virginia.

After removal of the sympathetic ganglia and trunks, the sympathectomized muscles appeared to suffer a diminution of the normal glycogen content, but if the fibers regenerated and sympathetic connections were reestablished, an augmentation of the glycogen store was noticed.

EFFECT OF SYMPATHECTOMY ON THE MUSCULATURE. H. E. BÜTTNER, Würzburg.

After sympathectomy, the author made the following observations: The arteries and capillaries dilated and the latter became more permeable; glycogen, lactic acid and ammonia increased; inorganic phosphorus content decreased; chronaxia and refractory phases were unaltered; fatigue was more easily elicited; the shortening state was increased.

PRESENCE OF SENSORY FIBERS IN THE INFERIOR LARYNGEAL NERVE TRUNK. C. M. CAMPOS and F. M. CAMPOS, S. Paulo.

By stimulating the intact nerve and the central end of the severed nerve, the authors obtained increase in blood pressure and stoppage of respirations, which they attribute to the presence of fibers running toward the central nervous system.

CONCERNING THE HYPOPHYSEAL (PARS DISTALIS) HORMONES FOR GROWTH AND REPRODUCTIVE PROCESSES. H. CUSHING and H. M. TEEL, Boston.

Experiments with injections into dogs confirmed the work of Smith and Evans on rats and mice that there are two distinct hormones in the anterior lobe, namely, the growth principle and the sex principle.

THE SYNDROME OF THE LOCAL STRYCHNINIZATION OF THE DORSAL SENSORY MECHANISMS OF THE SPINAL CORD. J. G. DUSSER DE BARENNE, Utrecht.

Experiments were conducted to throw light on the question as to whether the deep structures (muscles, tendons, periosteum) participate in the syndrome of strychninization of the spinal sensory mechanisms. It was found that the same reactions occurred on mechanical stimulation of deeper structures (cutaneous sensibility having been destroyed by section of the nerves to the skin) as when skin (with intact nerves) was stimulated. The strychninization syndrome was described as follows: (1) paroxysmal, paresthetic disturbances, occurring without any external stimulus, and even after dorsal root section; (2) hyperesthesia and hyperalgesia of skin and deeper structures in the strychninized segments; (3) hypereflexia.

EMOTIONAL DISTURBANCES FOLLOWING EXPERIMENTAL LESIONS OF THE BASE OF THE BRAIN (PRECHIASMAL). J. F. FULTON and F. D. INGRAHAM, Oxford.

To confirm the belief that the frontal lobes give rise to fiber tracts passing to the centers in the hypothalamus, the authors made an incision in the brain from 3 to 4 mm. anterior to the optic chiasm, from 2 to 3 mm. in depth, and extending from the midline to the olfactory radiation. As a result they noticed an immediate change in the disposition of cats, i. e., previously friendly and playful cats became ill-tempered. Gentle stroking evoked spitting, scratching and biting, accompanied by diffuse signs of sympathetic stimulation, e. g., dilatation of the pupils, sweating and pilomotor reaction. These results, they attributed to release of hypothalamic centers from inhibitory control of the frontal lobes.

THE MECHANISM OF SLEEP. W. R. HESS, Zürich.

A special method was developed in which the kind of electrical impulse and the shape of the electrodes played an essential part. By electrical excitation of a certain part of the brain, an inhibitory state similar to sleep was obtained.

The author also studied the brain to determine the localization of the parts inducing sleep. He pointed out that there is no localized sleep center, but that the areas producing sleep, when stimulated, were localized along the axis of the brain and adjacent to the ventricles. Emphasis is laid on the fact that sleep is the consequence of a stage of excitation, and that sleep is a positive process, promoting the restorative processes within tissues, and not a negative one, i. e., extinction of functional potencies. He concludes that sleep regulation belongs to the sphere of the vegetative functions and is on a level with the vegetative reflex functions.

VARIATIONS IN THE BASAL METABOLIC RATE APPARENTLY CAUSED BY THE MENTAL STATE OF THE SUBJECT. F. A. HITCHCOCK, Columbus, Ohio.

The author reports two cases in which daily basal metabolic rate determinations were made. In one patient undergoing a mental strain attendant on examinations for the degree of Doctor of Philosophy, the average basal rate was 40.12 calories per square meter of body surface. Four weeks later the average was 35.89 calories.

In another subject the basal rate jumped from 32.6 to 42.35 calories attendant on some mental excitement due to her work.

THE INFLUENCE OF PREGNANCY ON THE VISUAL FIELDS. J. P. JOHNS and A. W. ROWE, Boston.

Twenty-five cases were followed through pregnancy and three months post partum. The visual fields, in the majority of cases, showed a definite concentric contraction for form and color with slight enlargement of the blind spot, but none showed any changes characteristic of pituitary pathology wherein enlargement is great enough to cause pressure on the chiasm. Roentgenographic studies of the sella gave negative results. The authors conclude that visual field changes reported in pregnancy are probably due to functional modification rather than to enlargement or vascular changes in the pituitary gland.

THE SEPARATION OF A NEW PHYSIOLOGICALLY ACTIVE PRINCIPLE OF THE SUPRARENAL GLAND. ALFRED E. KOEHLER and LILLIAN EICHELBERGER, Chicago.

An epinephrine-free substance has been separated from the suprarenal gland, that is capable of elevating the basal metabolic rate and producing improvement in the various types of asthenias. Two processes of separation were described: one depending on the precipitation of the active principle with protein, the other by extraction with the lipoid fraction.

METABOLIC STUDIES FOLLOWING THE ADMINISTRATION OF SUPRARENAL EXTRACTS. ALFRED E. KOEHLER and A. BAIRD HASTINGS, Chicago.

The epinephrine-free extracts of the suprarenal gland raised the metabolism of dogs and mice when administered orally. The calorigenic effect on human subjects, with a low metabolic rate, was marked and a low mechanical efficiency was raised to normal. This effect is explained as due to more efficient utilization of carbohydrates and sparing of proteins.

CHRONAXIA OF SUBORDINATION AS DETERMINED BY POSTURE. L. LAPICQUE and M. LAPICQUE, Paris.

In a motor nerve severed from nervous centers, there is a definite chronaxia. This chronaxia, which is related to the diameter of the fiber and to the colloidal properties of the protoplasm, is called constitutional chronaxia. But in a spinal motor nerve having natural connections with nerve-centers, chronaxia is variable, generally shortened with regard to its constitutional value. This chronaxia, which is modified by a central action, is called the chronaxia of subordination.

The chronaxia of subordination is, to a great extent, governed reflexly, the chief afferent stimulation being the tension of the muscle. It is shortened when the muscle is stretched in posture changes, as it is also shortened when the dissected muscle is stretched. Severing of the nerve abolished any influence of posture or stretching.

AN EXAMINATION OF PAVLOV'S THEORY OF INTERNAL INHIBITION. H. S. LIDDELL, O. D. ANDERSON and W. T. JAMES, Ithaca, New York.

These investigators, working with sheep, made observations which supported Pavlov's theory of internal or cerebral inhibition. They also found that when a new adjustment required inhibition beyond the capacity of the brain of the sheep, "experimental neuroses" resulted. They, however, did not obtain results confirming Pavlov's conception of sleep as the summation and irradiation of internal inhibition.

THE SURFACE TICKLE SENSE OF THE HUMAN SKIN. WARREN P. LOMBARD, Ann Arbor.

The author retracts his previous statement of the specificity of tickle and touch spots in the skin and states that the evidence he has now obtained indicates

that the responses from some spots are constant, while the sensations from other spots vary according to the condition of the peripheral and central nervous mechanism.

THE MECHANISM OF REINFORCEMENT OF THE KNEE JERK IN THE HUMAN SUBJECT BY A NEW PROCEDURE. ARNO B. LUCKHARDT and MARY MONTGOMERY, Chicago.

The authors propose as a method for augmenting the knee jerk that the subject be instructed to hold the arm at right angles to the body, with or without a heavy article in the hand. They explain the increased response as due to increased tone in the quadriceps, as a result of an overflow of motor impulses to the knee jerk center.

REACTION OF SMOOTH MUSCLE TO STIMULATION OF THE VAGUS AND SYMPATHETIC NERVES IN ISOLATED NERVE MUSCLE PREPARATIONS. B. A. MCSWINEY and J. M. ROBSON, Leeds.

The authors found that stimulation of the vagus caused contraction of the muscle in practically all experiments. Changes in the frequency or strength of the current had no effect on the contraction, but after addition of atropine stimulation of the vagus caused relaxation of the muscle. The response to sympathetic stimulation varied. If the muscle relaxed on stimulation of the nerve with a high frequency current, contraction would be obtained on decreasing the strength or frequency of the current. On the other hand, if the first response was contraction of the muscle, variation of the strength or frequency of the current did not change the response. The response was abolished by ergotoxine.

INHIBITION IN THE NORMAL ACTIVITY OF THE CEREBRAL HEMISPHERES. I. P. PAVLOV, Leningrad.

In studying the activity of the cerebral hemispheres by his method of conditioned reflexes, Pavlov noted the continual participation of the process of inhibition. He considered that this inhibition serves two purposes, first to protect cortical cells from excessive functional destruction, and second, to protect these cells from useless work. He noted that if cortical irritability was raised by caffeine, or the stimulus was very strong, the inhibition was interfered with. But, on the other hand, whenever the conditioned stimulus as a signal was not accompanied by the unconditioned stimulus, or whenever the latter did not appear at the proper time, the inhibition rapidly appeared. The administration of bromide markedly increased the action of the inhibition in all cases.

THE DOG WITHOUT THE CEREBRUM. S. S. POLTYREV and G. P. ZELIONY, Leningrad.

The authors extirpated all of the brain above the corpora striata except for a small portion of the temporal lobes. After recovery, the behavior of the animals was typical of decerebrate animals. Attempts to establish conditioned reflexes with a metronome were unsuccessful, but a reflex could be established with a hunting horn.

EVIDENCE THAT THE POSTURAL TONUS OF DECEREBRATE RIGIDITY INCREASES IN AMOUNT BY THE SUCCESSIVE INNERVATION OF SINGLE MOTOR NEURONES. EUGENE L. PORTER, Galveston.

The author, working with one of the small muscles in the extensor caudae lateralis of a decerebrate cat, found that in passing from rest into tonic contraction, the record showed a series of sharp steps, just as was the result when the muscle was used in a nerve-muscle preparation with the nerve stimulated by gradual increase of the strength of the current. He concludes, that tonic contraction of decerebrate rigidity increased in amount by the innervation of one motor neuron

after another, with the resulting contraction of the muscle fibers innervated by each neuron.

On the Regulation of the Normal Water Intake in Rats and Its Experimental Modification Through Brain Punctures (Experimental Diabetes Insipidus). C. P. Richter and M. E. Brailey, Baltimore.

The authors measured the water intake in normal rats of various ages and found it to be related to body surface and about 800 cc. per square meter of body surface per day. For man, their figures would average about 1,500 cc. per day. They suggest that possibly the figure is applicable to all mammals. Lesions were made in the base of the brain in the region of the sella turcica. In thirteen of forty animals an increased water intake resulted, which was permanent. In one animal the water intake increased from 25 to 260 cc. per day.

The Effects of Sympathetic Ganglionectomy and Ramisectomy in Arthritis. Leonard G. Rowntree and Alfred W. Adson, Rochester, Minn.

The authors thought that there was some relationship between excessive vasoconstriction and arthritic symptoms. In an advanced case of arthritis deformans they removed the second, third and fourth lumbar sympathetic ganglia on both sides with immediate and complete cure of the arthritis. The relief has persisted for three years. Two years later, arthritic symptoms in the upper extremities became so severe in the same patient, that she returned for removal of the first and second dorsal ganglia and cervicodorsal ganglia on both sides. The result was an almost complete disappearance of the arthritis in both upper extremities.

Pharmacologic and Physiologic Studies on the Autonomic Nervous System. William Salant, Cold Spring Harbor, New York.

The author has studied the effects of salts of mercury and has shown that they increase the irritability of the parasympathetic system.

The Gaseous Metabolism of Nerves During and Following Anaerobiosis. Francis O. Schmitt, Berlin-Dahlem.

Using differential manometers and a new type of vessel, both the oxygen consumption and the carbon dioxide production of nerves were measured on the same fiber. They confirmed the fact that nerves incurred an oxygen debt in asphyxia, and the effect of stimulation and of chemicals on this debt was studied.

The Pontobulbar Vasomotor Center. J. M. Duncan Scott, Saskatoon.

With a Clarke's stereotaxic instrument carrying a capillary electrode for extremely weak unipolar stimulation, the brain stems of decerebrate cats were searched for a vasomotor center. The results were controlled by observing the electrical changes, shown by the most reactive spots when a rise of blood pressure was produced reflexly.

Rôle and Function of the Endothelium of the Capillary Walls ("barrières histio-hématiques") in Various Physiologic and Pathologic Conditions. L. Stern, Moscow.

The endothelium of the capillary walls is the anatomic barrier. The effectiveness of this barrier is changed by asphyxia, avitaminosis, inanition, changes in blood p_H, and intoxications.

Some Effects of Denervation on Muscular Contraction. H. C. Stevens and J. M. Rogoff, Cleveland.

Studies were made on the effect of the severing of sciatic nerves on the contraction of the gastrocnemius muscle of the frog. The denervated muscles showed a

slight degree of contracture, a slower response to stimulation, a tendency to staircase and quicker relaxation. The bearing of these observations on the mechanics of muscular contraction was discussed. An apparatus for measuring muscular tension was demonstrated.

VAGUS CHRONAXIA IN DOGS SENSITIZED TO HORSE SERUM AND MODIFICATION OF ANAPHYLACTIC REACTION FOLLOWING FARADIZATION OF THE VAGUS. O. O. STOLAND, N. P. SHERWOOD and R. A. WOODBURY, Kansas City.

On the bases of their results, the authors concluded that sensitizing doses of horse serum given to dogs, caused a reduction of chronaxia of the vagus nerve, and that stimulation of the vagus nerve caused a modification of the anaphylactic reaction.

A METHOD OF RECORDING THE RESPONSES OF INDIVIDUAL MUSCLES TO APPROPRIATE STIMULATION OF THE SEMICIRCULAR CANALS. JOHN TAIT and W. J. MCNALLY.

The author divided a decerebrate frog into two components, a leg component and a head-body component, connected only by the sciatic nerve. With intact labyrinths, sudden movements of the head-body component caused twitches of the leg component. These twitches of the leg-component would not occur if the head-body component was delabyrinthized.

CITRIC ACID IN ANIMAL FLUIDS. T. THUNBERG, Lund.

A method is described and the results in various fluids are given. In the cerebrospinal fluid the normal content is from 0.5 to 0.6 per thousand.

THE OXYTOCIC SUBSTANCE OF CEREBROSPINAL FLUID. H. B. VAN DYKE, PERCIVAL BAILEY and PAUL BUCY, Chicago.

The authors found that if care was exercised in keeping the calcium ion concentration of the artificial fluid and the cerebrospinal fluid bathing the isolated guinea-pig's uterus similar, no oxytocic substance could be found in the cerebrospinal fluid. But, if the cerebrospinal fluid contained from 0.2 to 0.7 mm. of calcium per liter more than the bath fluid, there was a marked oxytocic effect. They believe, therefore, that the positive or negative results of previous workers depended on the relation of the ionic concentration (particularly the calcium ion) of the artificial solution chosen to the ionic concentration of the spinal fluid.

THE ACTIVE NATURE OF THE INHIBITORY PROCESS AND THE IDENTITY OF ALL KINDS OF INHIBITION IN CONDITIONED REFLEXES. GEORGE W. VOLBORTH, Kharkov.

Using Pavlov's method of salivary conditioned reflexes the author established that a neutral external stimulus, when repeatedly coinciding in time with the process of inhibition in the hemispheres, becomes able to provoke the inhibition. Up to these experiments the state of positive induction had been observed only after the process of internal inhibition. Its appearance after the external inhibition is a strong support of Pavlov's view that the process by which the inhibition is brought about is identical in both cases in the internal and external inhibition.

OBSERVATIONS ON THE OXYTOCIC ACTIVITY OF CEREBROSPINAL FLUID. R. W. WHITEHEAD and M. H. REES, Denver.

The authors found the following: the cerebrospinal fluid removed from anesthetized dogs contained no oxytocic principle when tested on the isolated uterus of a guinea-pig. The injection of an estrus-inducing hormone caused no change in the fluid. The cerebrospinal fluid from unanesthetized dogs showed a very slight amount of oxytocic principle. This could be increased by administration of ovarian hormone. The fluid removed from female dogs immediately post partum showed a marked oxytocic activity.

Book Reviews

THE CASE OF MISS R. THE INTERPRETATION OF A LIFE STORY. By ALFRED ADLER. Translated by Eleanore and Friedrich Jensen. Price, $3.50. Pp. 306. New York: Greenberg, 1929.

The behavior of psychoneurotic patients is so complicated that formulations of the essential points of an individual case vary widely according to different psychopathologic points of view. Undoubtedly there are chains of events in neurotic developments to which the chief tenets of Adler's individual psychology are well fitted. The question is only how frequent the cases are which are best understood on this plane of neurotic "arrangements" (Adler). This presentation of the case of Miss R affords an excellent opportunity for an unbiased acquaintance with the author's individual psychology in action, showing at once its strength and weaknesses.

The history of the patient, as she wrote it down herself, is given in full, interspersed throughout with Dr. Adler's comments. He states expressly that he has never seen the patient. He gives interpretations of each sentence or paragraph of the patient's story as if she were in his office and telling it to him for the first time. His considerations and explanations are given extemporaneously, and he has "no more knowledge of the facts than are available to the reader."

The case concerns a young woman, the illegitimate daughter of poor parents who lived in two rooms. The father was a tailor; the mother helped him. There was a half-sister, the daughter of the mother by a previous husband. The patient was very much spoiled by her parents, especially by her father. She was nursed until 5 years of age. (It must be remembered that the whole history is given according to the patient's account.) Menses began at 17. She was apparently always given to "nervous" digestive upsets and more or less frequent loss of urinary control. When the father was dying, the mother insisted on a marriage ceremony to legitimatize the patient. The marriage was performed by the priest, and the father, exhausted by the ceremony, died soon after. At that time, the patient was about 18.

The patient's story covers the period from early childhood to a little less than 18 years of age. The home situation, her playmates, her likes and dislikes, her vanities, jealousies and fears, her early reactions to sexual matters — all are recorded in her own words. As a child she cultivated the habit of demanding of her parents much attention to her health. She tells of having whooping cough which lasted for a year, the last six months being spent in recovering from it. She was afraid at night, and suffered from insomnia at the age of 6 or 7. During pre-school age she felt compelled to call her parents and God bad names inwardly. She developed an obsessive-compulsive condition at the age of 14: a compulsion to swear was followed successively by obsessive fears of her eyes being injured by sunlight, of her teeth being broken or otherwise harmed, of contracting lupus, of breaking mirrors, stepping on certain spots or riding on certain cars, etc. Hand and body washing compulsions were also conspicuous.

Dr. Adler's interpretation reduces the case to a simple formula: ". . . . we can anticipate precisely what she is going to do or not to do according to the style of life developed. . . . She collects reasons to avoid love in which she fears a defeat" (page 145). ". . . . We see her energetically occupied in establishing between herself and the community a barrier, a waste heap. She feels compelled to curse God and her relatives, reproaches herself when she is depressed, rules her environment and wastes her time with useless things. Like every neurotic, she uses her neurosis in order to be able to say: I have not been able to solve my life problems, because I have been so overburdened with these things. This 'because' is typical. It is the neurotic justification in a special logic which is arranged to evade the true logic of life and to fit the patient's needs. Every person

with some common sense can see how weak this justification is. And yet the neurotic must believe in it as he believes in something holy, whereby he gives one to understand that in him is some glimmering of the distance between his conduct and the real demands of communal life. Otherwise why should he have to justify himself?" (page 177). ". . . . This girl's psyche resorts to all sorts of artifices to overcome real and imaginary difficulties of life . . . the nervous psyche is forced to make use of such tricks and artifices in order to be able even to approach the fictive, tension-producing goal" (page 280).

Of far greater interest than this fitting of a case into a theory are the many comments of Dr. Adler on details of the history. There are many ingenious observations and remarks based on the patient's statements which are distinctly worth reading, but which do not lend themselves to survey in a review. The book furnishes a good illustration of Adler's method of interpretation. His general manner of approach seems to be better than his creed. Giving all due credit to the ingeniousness of the interpretations, one becomes at the end a little dubious about a method which deduces so much from so little, and one is not convinced by the superstructure of analysis built on an incomplete case history by an orgy of clever interpretation.

The book seems rather loosely and quickly put together, but this seeming defect adds to its interest. Here is a frank statement by a psychopathologist about his reactions to a case history as it evolves sentence by sentence. It would be of great interest if others would give similar statements — in connection with actual cases — of their psychologic methods and points of view. Adler's book confirms the opinion that there are cases in which neurotic behavior is explicable on the basis of the mechanisms which he has evolved — although strangely enough, the case of Miss R does not seem to belong to this group, unless one jams the facts into a Procrustes bed.

The book has a good brief introduction by the editor, in which the chief tenets of Adler's psychology are lucidly set forth. The translation is excellent. The slightly pornographically tinged blurb of the publisher ("No detail is spared") is unfortunate and misleading for what is after all a serious and valuable book.

INTRODUCTION TO THE TECHNIC OF CHILD ANALYSIS. By ANNA FREUD, Vienna. Authorized Translation Supervised by L. PIERCE CLARK, M.D. Price, $1.50. Pp. 58. Washington, D. C.: Nervous and Mental Disease Publishing Company, 1928.

The monograph is a reproduction of four lectures delivered before the Vienna Psychoanalytical Society and is based on a protracted psychoanalytic study of ten children.

In the first lecture, "The Introduction to Child Analysis," the author insists that the treatment should be restricted to patients with definite infantile neuroses. She next stresses the great differences between psychoanalysis of the child and that of the adult. The adult has some knowledge of his difficulties and applies for treatment of his own accord, which is not the case with the child. The first step is to prepare the patient for analysis — to find a point of attack. While a few of the children had some desire to correct undesirable traits and fell easily into rapport, the majority had no desire to make friends and some were openly antagonistic. In these difficult cases, Anna Freud resorted to strategy which gained confidence or rendered her indispensable or at least interesting to the mental life of the children; this gradually brought them to a realization of the existing difficulties and developed a desire to correct them.

In the second lecture, the author discusses the methods of child analysis. It requires serious modification of the method used with adults. It requires not only unusual tact and intuition but the utilization of a great many tricks. The indifference and rigidity practiced in the analysis of the adult must give way to a childish friendliness and understanding. Conscious recollections, which is one of the four technical approaches in the adult, is not available in the child and must be substituted by a history from the family which is frequently inaccurate and distorted.

On the other hand, dream analysis, the second technical approach, is not only applicable but in most cases even more effective than in the adult, for dreams are more real to the child. In addition, the utilization of day dreams, of "continuous stories" and of drawing is stressed and profusely illustrated, and shows an important path to the unconscious of the child. The difficult modification of free association — the third technical approach in analysis — is discussed at length. The child will not associate readily and will soon tire and discontinue. Of the various substitutes for free association, that of Hug-Hellmuth of games in the child's home environment and that of Frau Melanie Klein of making up stories with toys, are utilized.

In the third lecture, the fourth approach of psychoanalytic technic, "The Rôle of Transference in Child Analysis," is discussed. Anna Freud holds to the opinion that no transference neurosis is established unless the child is removed from the home, when the analyst may become the object of positive and negative transference. At most, the analyst in the extramural treatment becomes a member of the family group. As such, the analyst insists on cooperation of the group, without which the treatment is futile. Harmony and cooperation on the part of the parents are indispensable.

The last lecture treats of "The Relation of Child Analysis to Education" and is probably the most interesting. The advantages and disadvantages of child analysis are summarized. It is rather disappointing to note that while the psychic content of the first two years of life are easier to penetrate, the prearticulate period remains dark. She concludes that this important period is better explored by free association and transference reactions which are poorly attainable in child analysis. The purpose of psychoanalysis is to elevate the conflicting tendencies of the instinctive, unconscious impulses of the ego and the super-ego to a level where the super-ego can be influenced. The child's super-ego being weak and dependent, the juvenile neurosis is more readily influenced by the outer world. A further consideration is the child's dual morality in respect to shame and disgust — one for the adult world and one for the child world. These factors transform the classic analyst into one who "not only educates and analyzes but also one who permits and forbids, loosens and holds in check again." After reviewing all these modifications and difficulties, the author cites three important possibilities of child neurosis: (1) The child has to retrace only a short distance to reach the normal path. (2) Correction of the super-ego is comparatively easy as the child neurosis results from conflicts centering around parental images which are alive and relatively vivid. (3) Modification of the child's environment is possible as the requirements of the child are relatively simple.

Considering the complexity of the subject, the lectures are exceedingly clear. The author is to be complimented on her truthfulness and acknowledgment of the many shortcomings of the procedure. Anyone interested in psychoanalysis and in child psychology will find this monograph extremely interesting.

LE SYNDROME EPILEPSIE. By O. CROUZON. Price, 55 francs. Pp. 268. Paris: Gaston Doin, 1929.

This book is an excellent symposium of the clinical aspects of epilepsy. The first part of the volume is devoted to a careful description of various phenomena composing the clinical syndrome. This is well done and comprises 108 pages. There are many references given by name to the work of other authors, but there is no bibliography showing where these works may be found. This is a distinct handicap to the usefulness of the book, and it is to be deplored that the author did not even put in the dates of the contributions by the various men quoted.

Part two deals with the etiology of epilepsy and is divided into: (*a*) general ideas of etiology, (*b*) the infantile epileptic syndrome, (*c*) the epileptic syndrome of childhood and adolescence and (*d*) the adult epileptic syndrome. All this is largely a listing of the various phenomena observed in order to group them and make some order from which an etiologic conclusion may be drawn. The epilepsy

that follows brain tumors is then discussed and also that found with inflammations of the brain. Only one page is given to a discussion of epilepsy arising from disturbances of the circulation, while there is a long discussion of those cases which are supposed to arise from reflex stimulation and from intoxications. There is a good discussion of the convulsions found in eclampsia gravidarum which throws light on the general possibilities of a chemical cause. Old age epilepsy and focal epilepsy are then discussed. Then later, under the name of the syndrome of Bravais-Jackson, the author states that Bravais described this syndrome in 1827, but gives no reference to the original contribution. There is then a discussion of differential diagnosis and of traumatic epilepsy. All this part is interesting, but the arguments as to etiology rest largely on clinical data.

In part three there is a discussion of the pathologic anatomy which brings out nothing new, although one is surprised to find no reference to the work of Spielmeyer and his collaborators.

In part four the pathologic physiology is discussed and here is an extended exposition of the evidence concerning "la toxicité des humeurs," and anaphylactic shock. It is evident that the author is especially interested in this aspect and leans toward believing that hemoclastic crisis caused by some unknown antigen may produce chemical changes which are responsible for the attacks. There is a long review of the various endocrine theories which is well done and critical, but once more the references are poorly documented and are not always well chosen. For example, under hypothesis there is no mention of the work of Cushing. The author believes that the endocrine glands have a general action on metabolism and that under their influence abnormality of internal secretion may lead to intoxication of the organism and an epileptic seizure; or it may be that abnormalities merely give a more favorable ground on which anaphylactic shock may work, but the author realizes that it is not proved that endocrine abnormalities are more marked among epileptic persons than among the general run of persons.

Under circulatory troubles as a cause of epilepsy there is an extremely brief description and more stress is made on the changes in the spinal fluid circulation than on those found in the arterial circulation.

Four theories as to the location of the focus of origin in the brain are discussed: (1) the idea that the seizures arise in the subcortical gray matter; (2) that they arise in the cerebral cortex; (3) that the autonomic nervous system is to blame, and (4) that the origin may be in the peripheral nerves giving rise to reflex changes. From a physiologic point of view these are inadequately discussed, and no reference is given to the important work of Foerster.

In the fifth part, the treatment for epilepsy in former times and the modern methods are discussed in detail. The book is closed with a brief chapter on medico-legal and social aspects of epilepsy. It is written in a clear and concise manner, and has an unquestionable, practical interest not only to the reader specializing in this particular field, but also to a general practitioner.

EXPERIMENTAL ANALYSIS OF THE SENSORI-MOTOR CONSEQUENCES OF PASSIVE OSCILLATION, ROTARY AND RECTILINEAR. By ROLAND C. TRAVIS and RAYMOND DODGE, Psychological Monograph 38, no. 3. Pp. 96. Princeton, N. J.: Psychological Review Company, 1928.

Sine-wave rotary and rectilinear oscillation provided the stimuli for the study of the sensitivity of the several vestibular organs. Voluntary, manual, compensatory movement of the arm and hand and, in the case of rotary oscillation, of the fingers was employed as means of response to the perception of oscillatory motion. The apparatus for rotary oscillation consisted of a rotating platform, a driving mechanism and a recording system. The rotating platform was the same as that used by Dodge in his previous studies of rotation. A rectilinear platform which was connected with the rotating platform and driving mechanism of the latter was used for rectilinear oscillation, and the platform was driven by the same Pathé-motor driving-rod mechanism. A recording system similar to that for rotary oscillation was employed. Two subjects (the writers) were used. Various predetermined

frequencies and amplitudes were employed in the case of both rotary and rectilinear oscillation. No sharp line was found between positive compensation, no compensation and negative compensation values. The average vestibular sensitivity to rotary oscillation for two subjects in terms of 50 per cent right responses with the subject at the axis was 0.48 degrees per second in average velocity. The corresponding average acceleration value was 0.0276 cm. per second. Analogous values for rectilinear oscillation are given for various positions of the body. In sine-wave oscillation, both rotary and rectilinear, the percentage of right responses was found to vary directly as the average velocity and average acceleration. Vestibular stimuli of constant intensity and frequency produced marked variability in the nature of voluntary manual compensations. The point at which response originates after the initiation of the stimuli varies markedly, the majority of responses occurring during the first quarter of the oscillation curve. As the frequency and intensity of stimulation decreased, summation of excitatory processes was more necessary to evoke a response. Motion tended to be perceived in the wrong direction at low intensities and frequencies of oscillation. As the frequency decreased the percentage of negative reactions occurring on the deceleration period increased. Visual cues permitted much finer adjustment and more improvement by practice in the adequacy of compensation than vestibular. When the head was used as the mobile member for voluntary compensation to oscillation, the compensation interrupted perception of motion, confirming the theory that the main receptors for rotary motion are localized in the head. The body, when free to move in a standing position, remains perpendicular but a small percentage of the time. Twenty-three per cent of body sway produced an adequate stimulus for the semicircular canals, which complicated the sensory data in the perception of rectilinear motion by introducing a rotary factor. There was found to be apparent rivalry between the rectilinear-rotary vestibular data and the kinesthetic in standing positions. Kinesthetic factors were found to be more than ten times more adequate than the vestibule in perception of rectilinear oscillation. The average velocity of the vestibular receptors for rotary oscillation was found to be 70 times greater than for rectilinear in terms of the average velocity of the bony labyrinth in the two situations, and 600 times greater in terms of average acceleration. This probably indicates two separate receptors for the perception of rotary and rectilinear oscillation respectively. The rectilinear component was predominant for one subject and the rotary for the other, under conditions of rotary oscillation with the subject at various distances from the axis. "It was shown that the gain from position to position in the percentage of right responses to the rotary component was not due to improvement by practice, but probably due to the elimination of an inhibitive effect of the rectilinear component."

HANDBUCH DER NEUROLOGIE DES OHRES. By PROF. DR. G. ALEXANDER, PROF. DR. O. MARBURG and DR. H. BRUNNER. Volume 2, part 2. Price, 150 Rm. Pp. 1227. Berlin: Urban & Schwarzenberg, 1929.

In 1923, the first volume of a series on the neurology of the ear appeared under the editorship of Prof. Dr. G. Alexander, Prof. Dr. O. Marburg and Dr. H. Brunner. Since then, three volumes have appeared, reviews of which were published in the ARCHIVES. The book under review is the second part of the second volume, the publication of which has apparently been delayed, for all others of the series have appeared. The subject matter is divided into three gross headings: (1) inflammatory diseases; (2) syphilis, and (3) tumors.

Under inflammations there are discussed, in order: inflammations of the inner ear, toxic neuritis of the eighth nerve, inflammatory nonpurulent diseases of the brain, the pathology of intracranial otogenic disease, extradural otogenic diseases, subdural otogenic diseases, otogenic infectious purulent meningo-encephalitis, otogenic abscesses of the temporal lobe, and otogenic cerebellar abscesses. Each subdivision has a separate author, although most of this division is under the authorship of Prof. Dr. G. Alexander and Dr. H. Brunner.

The subjects discussed under the different subdivisions are most complete. For example, under the heading nonpurulent inflammations of the brain, the following topics are discussed: epidemic encephalitis, in which there is a complete discussion of the history, epidemiology, pathologic anatomy, symptomatology, differential diagnosis, therapy, etc., with references to the literature, the whole taking about 100 pages. In the next subject, under inflammations of the brain, are given the allied infectious toxic diseases such as acute epidemic poliomyelitis, epidemic encephalitis, malarial encephalitis, other types of infectious encephalitis, acute and subacute primary cortical encephalitis and Wernicke's "polioencephalitis haemorrhagica superior." The third subdivision deals with multiple and other types of sclerosis.

Under syphilis, involvement of the eighth nerve and of other parts of the nervous system in relation to the eighth nerve are discussed. There are three subdivisions under tumors: (1) symptoms in relation to the cochlear and labyrinthine apparatus in neoplasms of the brain and resulting from brain pressure; (2) disturbances of speech in lesions of the temporal lobe, and (3) tumors of the temporal lobe.

As has been said in previous reviews the work is most thoroughly done and the entire neurologic and otologic professions are indebted to the authors for the consummation of this monumental work. No neurologist at all interested in the ear can afford to be without these volumes.

SUBORDINATION AUTORITÄT PSYCHOTHERAPIE: EINE STUDIE VOM STANDPUNKT DES KLINISCHEN EMPIRIKERS By ERWIN STRANSKY, M.D. Paper. Price, 4.80 marks. Pp. 70. Berlin: Julius Springer, 1928.

Writing as a practicing physician who is dealing with the treatment of patients and basing his conclusions on studies of a number of patients over a long period, Stransky endeavors to show that, in actual practice, conflicts between the patient and his environment are of far greater moment than those of a sexual nature. He regards the struggle for supremacy as a primary urge. In childhood there is a conflict between the authority of the parents and the subordination of the child; later, a similar situation exists between the child and the teacher, and still later, between each person and those around him. These conflicts are not sexual or oedipus complexes but are matters of subordination and authority, which Stransky designates as the SAR or subordination-authority-relation. In the neurotic patients studied, for example, the principal and almost stereotyped complaints concerned unhappinesses in the home. The triad "a brutal, drunken father (somewhat less frequently a loveless mother or stepmother; or the child orphaned and thrust out among strangers), oppression and hunger in the family, the early need to undertake hard or tiresome work under bodily or mental ill treatment and deprivation" was found to be extremely common. These experiences of childhood and youth reappear often in the form of transsexual complaints, but they are not primarily sexual.

In the relations between physician and patient, again, this same problem of SAR arises, a relation that includes what is spoken of as transference by psychoanalysts. On the handling of this problem depends much of the success that can be secured in the management and readjustment of the patient. Stransky reports the results he has secured with a group of patients observed in a clinic during a five year period and discusses in detail the technic and analysis of the situations. He recognizes fully the importance of the anlage of the personality.

The book is an extremely interesting study, eminently practical in its bearings and thoroughly worth the attention of every psychiatrist.

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